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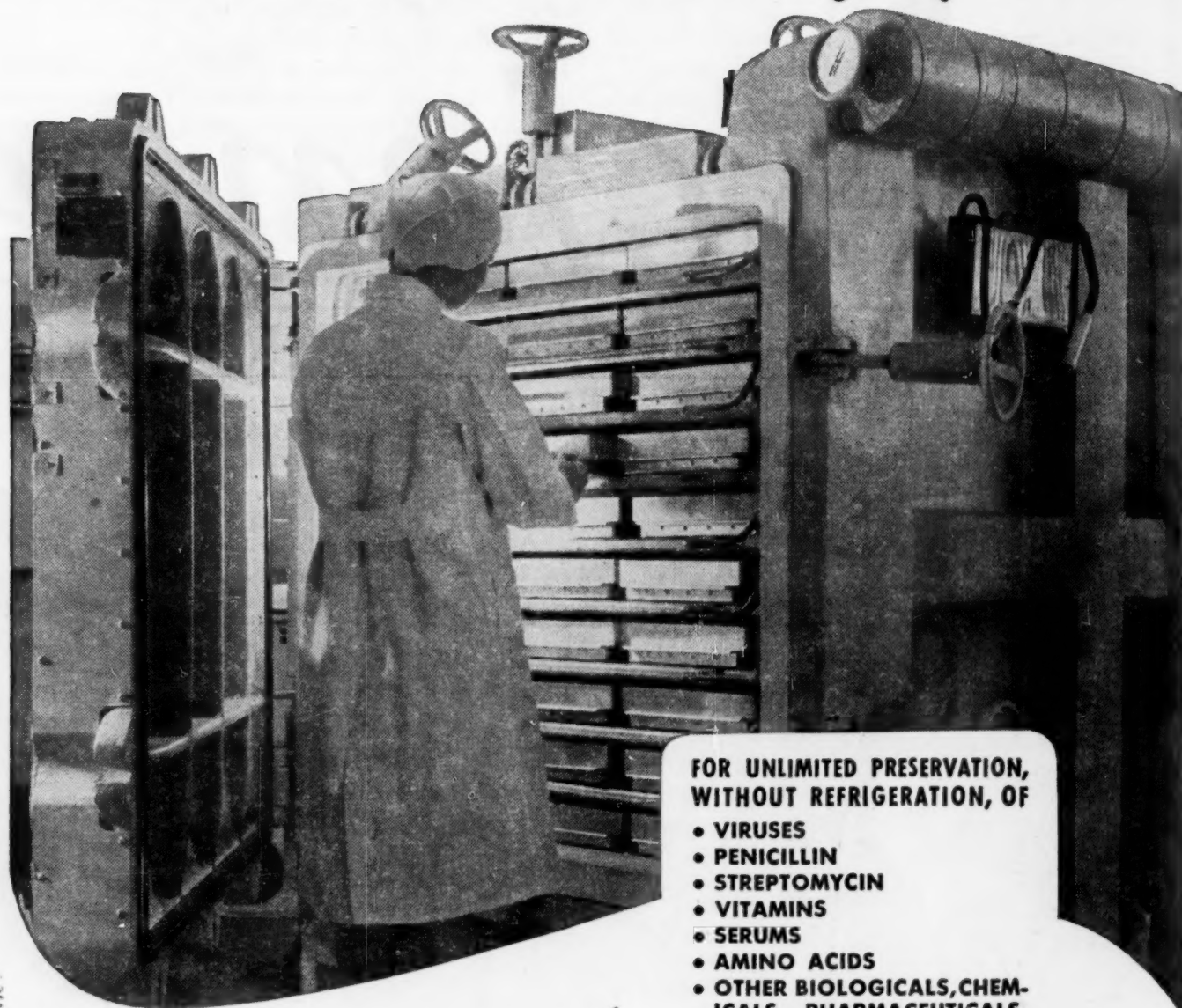


President Truman congratulating 10 key scientists for their work in the wartime Office of Scientific Research and Development, January 20. Left to right, seated: James B. Conant, president, Harvard University; the President; and Alfred N. Richards, vice-president, University of Pennsylvania. Standing: Karl T. Compton, president, Massachusetts Institute of Technology; Lewis H. Weed, chairman, Division of Medical Sciences, National Research Council; Vannevar Bush, chairman, new Army-Navy Joint Research and Development Board; Frank B. Jewett, president, National Academy of Sciences; J. C. Hunsaker, Massachusetts Institute of Technology; Roger Adams, University of Illinois; A. Baird Hastings, Harvard University; and A. R. Dochez, Columbia University. Richard C. Tolman, California Institute of Technology, who also received a letter of thanks from President Truman, was not in Washington.

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Work of Soviet Biologists
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Work of Soviet Biologists:

Theoretical Genetics

N. P. Dubinin, *Institute of Experimental Biology,
Academy of Sciences, Moscow, U.S.S.R.*

PROBLEMS OF THEORETICAL GENETICS are of exceptional importance for the development of the science of life and in elaborating methods of controlling the evolution of agricultural plants and domestic animals.

The succession of all organic forms is determined by heredity. Every animal and plant develops from an original cell, and it is clear, therefore, that the system of heredity must form an important part of this cell, since the entire process of development rests upon it. The persistence of characters of both the species and the individual through many generations is based on the innermost peculiarities of the material cellular organization of the fertilized egg. Variations in this organization present the material for the evolution and selection of organisms.

The researches of Boveri, Wilson, and Morgan showed that heredity rests, in the first place, in the cell nucleus, consisting of separate segments called chromosomes, and is connected with the transmission of certain specific substances contained in them. Development and hereditary variation are caused by metabolism between the chromosomes and cytoplasm of the cell. This shows that the problem of molecular organization of chromosomes and metabolism between the chromosomes and the cytoplasm is the central one in theoretical genetics, as well as for the solution of the entire question relating to the organization of living matter and the origin of life.

Of special importance in analyzing problems of heredity is the historical method used to solve the questions of the evolution of hereditary forms in serious changes of organisms, the evolution of genetic systems during the processes of formation of species, and the evolution of species of plants and animals. The great range and depth of modern problems of theoretical genetics have given rise to many synthetic methods combining the materials and methods of genetics, cytology, physics, chemistry, mathematics, and the theory of evolution.

The elucidation of problems of evolutionary genetics played an important role in the history and development of Soviet genetics. This trend was originated and evolved in the works of Russian scientists. The pioneer of experimental research in the genetics of population was S. S. Chetverykov, who in 1926 published a work

entitled *Certain factors of the evolutionary theory from the point of view of modern genetics*. In 1928-29 Chetverykov published a short, preliminary report on experimental analysis of the wild population of *Drosophila melanogaster* from Gelendjik. Beginning in 1930, the writer and his laboratory staff carried out a number of experiments connected with new questions of the genetics of populations with regard to both the mutation of genes and the evolutionary structure of chromosomes. At about the same time a number of important works by D. D. Romashev and his assistants appeared.

These researches served as a source for the development of the comprehensive Soviet school of evolutionary genetics, and works on this subject were published by S. M. Gershenson and his laboratory staff, R. L. Berg, N. N. Sokolov, G. G. Tinyakov, Y. M. Olenov, G. D. Muretov, and others.

After the appearance of the above-mentioned researches, the new tendency rapidly assumed the nature of one of the central trends in world genetics. In the United States, Dobzhansky, Sturtevant, and other scientists published important contributions to the genetics of populations and the general theory of the origin of species. The works of Gordon appeared in Great Britain, of Timofeyev-Ressovsky in Germany, etc.

The initial discovery, serving as the source for this entire trend, was the establishment of the fact that populations of wild species possess vast, historically accumulated reserves of hereditary variability, a considerable part of these reserves being hidden in the populations in a heterozygous state (Chetverykov, Dubinin). The new hereditary changes which appear in each generation and the system of historically accumulated variability became the center around which works on genetics and evolution of populations revolved. The honor of formulating the rule that a genetical analysis of the processes of the origin of species must be based on the theory of corpuscular heredity in populations belongs to S. S. Chetverykov (1926). This was an important principle in creating new teachings about the factors of evolution and methods of selection.

Just as chemistry and physics were founded on Dalton's theory (1802) of the atomic structure of matter and as genetics was founded on Mendel's law (1866), the theory of evolution received a new basis for the development of the teachings on the origin of species in the theory of the corpuscular system of hereditary

variability in populations. This idea was also developed by Fisher in England in 1930, in his well-known book, *The genetical theory of natural selection*.

Experimental research into natural selection in nature encountered great difficulties. The first work on this subject was that of V. N. Sukachev, who in 1927 made a study of the competition between genotypically different forms of dandelions taken from various localities. Pisarev (1923) and Sapegin (1922) studied the struggle for existence in fields sown with different varieties of wheat. In 1941 Gershenson made an attempt to study natural selection in wild populations of *Drosophila*. Unexpected possibilities were suddenly disclosed in Dubinin's and Tinyakov's paper (1946) on the structural evolution of the nucleus in natural populations of *Drosophila funebris*.

Inversions, which represent the chief types of structural changes of the chromosomes, proved to be environmentally controlled. The rate of evolution of populations proved to be very rapid against the background of the changes introduced by man's interference. The species was divided into chromosomal-ecological urban and rural races. The processes of divergence of these races under the experimental influence of natural selection could be reproduced both in the laboratory and in nature. The sharp influence of war on the chromosomal structure of populations, as well as the climatic gradients in the distribution of various inversions in populations from the north to the south, and the transitional zones between populations of the central urban and the rural races, were ascertained. This work opened up new fields including analysis of the actual influence of natural selection, study of the roles played by migration and isolation, and use of natural selection for experimental purposes.

A different approach to the problems of evolution of plants was found by N. I. Vavilov, who in the course of 20 years carried out highly important genetical and ecological research, classification, and selection work on cultivated plants, covering all the chief world centers of origin of these plants. He has given us highly important conceptions of homologous variability, of hereditary immunity in wheat, and of other problems in genetics, selection, and evolution. The work on geographical distribution of wheat is now being continued by T. K. Lepin.

The phenomena of polyploidy, *i.e.* the multiple increase of the chromosomes in a nucleus, is of great importance in the evolution of plants in nature, in ascertaining the origin of cultivated plants, and in selection. New methods of controlling evolution and selection by experimentally caused polyploidy were evolved in Russia in 1902 by Gerasimov in the course of his remarkable experiments. By influencing the cells of *Spirogyra* (fresh-water algae), by means of narcotics and other factors, Gerasimov caused artificial doubling of the

nucleus mass (autopolyploidy). He also discovered autopolyploidic races with doubled chromosome masses in nature.

The works of G. D. Karpechenko (1925-40) proved that doubling the number of chromosomes in sterile hybrids obtained from interspecific crosses leads to the appearance of fruitful forms. His classic example of the cabbage-radish hybrid established the basic principles of allopolyploidy (doubling the number of chromosomes in hybrids).

Following Blakeslee's and Avery's discovery (1937) that colchicine is a powerful medium for the artificial derivation of polyploids, numerous experiments were carried out in this field in the U.S.S.R. Of these, only the successful application of the polyploid method in selection work and in propagating new varieties of cultivated plants will be mentioned here.

Between 1941-46 V. V. Sakharov, S. L. Frolova, and V. V. Mansurova obtained an autotetraploid variety of buckwheat with 32 chromosomes instead of 16. This is a large, evenly developed plant with surprisingly large grains. The crop yield of tetraploid buckwheat is one and a half or twice that of the ordinary variety, the flowers have an increased nectar content, etc. This plant presents exceptionally favorable material for further selection of varieties with a great number of chromosomes.

M. S. Navashin obtained a tetraploid form of the kok-sagyz rubber plant through the action of colchicine. The new variety has roots 1.6 times larger than the old, resulting in an accordingly higher rubber yield, large seeds with increased strength of germination, larger rubber granules in the latex, an easier flow of sap from the roots because of the larger size of the latex vessels, a higher crop yield, and so on.

A. R. Zhebrak, utilizing colchicine, has carried out a great deal of work connected with the synthesis of new varieties and species of wheat (1938-46). Particularly interesting among these is the variety known as Timofeyev wheat, discovered by P. M. Zhukovsky in the Caucasian Mountains. This variety is hardy and has good resistance to the majority of plant diseases. Zhebrak crossed Timofeyev wheat with many ecological-geographical races of 28-chromosomal wheats of 5 different species from Abyssinia, Algiers, Morocco, Turkey, America, and other countries and as a result a new species of wheat with 5 subspecies and 32 varieties was propagated. By crossing this species with 42-chromosomal and 14-chromosomal species and after doubling the chromosomes in the sterile hybrids, Zhebrak obtained new 42- and 70-chromosomal species. Species of wheat with 56 and 70 chromosomes were hitherto unknown in nature. At the end of Zhebrak's book, *The synthesis of new species of wheat* (published in 1944), the author writes: "In view of the new data about artificial polyploidia we may state that modern experi-

mental cytogenetics has achieved a great end—the synthesis of new species of cultivated plants.”

The problem of extraspecies crossing of plants is also being dealt with by N. V. Tsitsin. Working in conjunction with V. E. Pisarev, Blakhsheyev, and others, Tsitsin succeeded in crossing wheat with *Elymus*. He is continuing analysis on the formation of varieties in hybrids of wheat and couch grass.

In 1928 N. K. Koltsov published his remarkable work on *The physical-chemical elements of morphology*, in which he outlined the concept of the molecular organization of chromosomes. This hypothesis formed the basis for one of the chief modern trends in genetics. According to Koltsov, the basis of a chromosome is the polypeptid chain, the separate radicals of which are genes. The most important part of this hypothesis touches upon the question of the reproduction of a chromosome. Koltsov proposed the theory of autocatalysis, according to which the chromosome does not split up, as was formerly supposed, but reproduces a double—a daughter—chromosome from the cytoplasmic substances, analogous to the growth of crystals. In his work, *The structure of chromosomes and their metabolism* (1938), Koltsov developed a number of highly important conceptions of the physical nature of the metabolism between the genes and the cytoplasm during the processes of reproduction of genes, and of the general nature of the metabolism between the chromosomes and the cytoplasm.

A. N. Belozersky proved the presence of complex proteins in the chromosomes of plants, which changes the hitherto prevalent opinion that only proteins of the type of protamines and histones participate in the structure of chromosomes. Belozersky's discovery coincided with the work of the Shtedmans in Great Britain on chromosomin. Belozersky (1945–46) developed an interesting theory on the evolution of nucleic acids, and the blockading effect of thymonucleic acid on the reactive groups of chromosome proteins and others.

Koltsov's hypothesis on the autocatalytic reproduction of genes is now the most widely accepted in world scientific circles. In 1945 Prokofieva attempted by cytogenetic methods to establish the difference between the mother chromosome and the daughter which had formed as the result of autocatalysis next to the former. Between 1941 and 1946 S. L. Frolova applied the methods of partial digestion of chromosomes by enzymes in order to ascertain the delicate structure of the former. In the U.S.S.R. Koltsov had laid the foundations of the teachings on the cytogenesis of the lower organisms; continuing this work, M. A. Peshkoff achieved considerable success when he showed the nuclear organization of chromatin in the bacterial cell. Along with the nuclear organization of chromatin in karyophan (discovered by him) and other bacteria, the nucleus proved to be peculiar also to other typical pathogenetic microbes.

These data are extremely important for an understanding of the forms of evolution of the organization of hereditary systems and the nature of the bacterial cell itself. Robino and other scientists subsequently arrived at the same conclusions in England.

The modern teaching on the morphology of chromosomes also originated in Russia, where it was based on the classic works of S. G. Navashin (1910–30). A number of his works indicated important trends in modern cytogenetics. This line of research is represented by many outstanding contributions by S. G. Navashin's pupils—G. A. Levitsky, M. S. Navashin, L. N. Delonay, L. N. Sveshnikova, N. T. Kakhidze, and others. Y. Elengorn (1940–46) has submitted interesting papers on the nature of meiosis, and D. F. Petrov (1940–46), on the nature of autotynthesis. The delicate structure of chromosomes is being investigated by A. A. Prokofieva. Research into the general cytology of heredity is being conducted by I. I. Sokolov, L. P. Breslavets, L. S. Pashkovsky, E. N. Gerasimova, and others.

A large group of scientists, including N. P. Dubinin, B. N. Sidorov, N. N. Sokolov, V. V. Sakharov, G. G. Tinyakov, I. A. Rapoport, M. L. Belgovsky, and V. V. Khvostova, are engaged in research into the nature of the gene, structural mutations of chromosomes, the phenomena of the effect resulting from the position of the genes, artificially caused mutations, sudden variation, etc. This work is being conducted chiefly on *Drosophyllum*. Mention must also be made of the organization of special roentgen-genetic laboratories in Moscow (1946) by S. N. Ardashnikov, N. I. Shapiro, and M. A. Arsenyeva, and in Leningrad (1946) by Y. M. Olenov and Solodovnikov.

Problems of phenogenetics are also engaging the attention of a number of scientists. Artificially caused morphosis was first effected in Moscow by G. G. Frizen, while the method of temperature morphosis was elaborated by Goldschmidt in America at the same time (1939). The parallelism of hereditary and nonhereditary variability discovered here enables us to judge the means of gene action on development. New successes were achieved by I. A. Rapoport in 1941–46 when he developed the method of homomorphosis and showed that almost all mutative variations can be caused (copied) by the action of certain chemical substances. N. N. Medvedev is working out methods of transplanting imaginal buds.

B. L. Astaurov is studying the cytogenetics of androgenesis and gynogenesis and the problem of relation between the nucleus and the cytoplasm in heredity. V. N. Natali and L. Y. Blyakher have studied methods of determining the sex of viviparous fishes. The former's latest work (1946) deals with differentiation of sex in teleost fishes. The author has shown a special type of medullocortical antagonism in the differentiation of the sex glands and draws a number of conclusions on

the forms of evolution of sex differentiation in fishes as compared with amphibians.

S. S. Chetverikov, V. P. Efroimson, and B. L. Astaurov are engaged in researches into the genetics and phenogenetics of the complicated phenomenon of voltinism in mulberry and oak silkworms.

Problems of the phenogenetics of behavior and instinct are being studied on dogs by L. V. Krushinsky, on birds by A. N. Promptov, and on *Drosophyllum* by R. A. Mazing. The majority of this work is being conducted in the Institute of Genetics of Nervous Activity, founded by I. N. Pavlov.

A new synthesis of genetics and evolutionary teachings is presented in various published papers by I. I. Shmalhausen. Highly interesting, also, are the experiments on correlation and selection, carried out in the laboratory of I. I. Shmalhausen and M. M. Kamshilov. The

question of the evolutionary importance of nonhereditary variability is being studied in great detail by I. I. Shmalhausen, V. S. Kirpichnikov, I. I. Lukin, G. F. Gause, and others. All these researches are building up a genetic foundation for Morgan's idea that adaptive modification paves the way to evolution. Shmalhausen's general teachings on the ways of the evolutionary process throw a new light on the conception of the importance of reactive correlative systems, the most important peculiarity of which is the ability for modificatory adaptations.

As has been shown in this short review, Soviet biologists are devoting much attention to the problems of genetics, which are among the most important confronting modern science. We are confident that we shall achieve further great progress in genetics in the near future.

Ultrashort Application Time of Penetrating Electrons:

A Tool for Sterilization and Preservation of Food in the Raw State¹

Arno Brasch and Wolfgang Huber

Research Laboratories, Electronized Chemicals Corporation, New York City

DURING THE LAST SEVERAL YEARS, in an attempt to determine the selective effects of ultrashort time exposures as compared with prolonged radiation periods, we have exposed a number of drugs and other chemical compounds, foodstuffs, and cultures of microorganisms to the action of penetrating, negatively charged particles (electrons), which were released during a time period of about 1/1,000,000 of a second. The electronic intensity applied during such short radiation impulses amounted to about 30,000–50,000 amperes.

It is a well-known fact that all chemical reactions need a certain starting time, and it remained to be seen if various desired biological effects could be exercised ahead of undesired chemical side reactions (5).

There exists today no convenient method of preserving foodstuffs in their fresh, raw state, and our experiments were in part directed to this need. Another aspect of the work involved the use of this radiation method in the field of bacteriology and medicine to determine whether we had at our disposal a more differentiated tool than was heretofore available in the treatment of microorganisms—as, for example, attenuation.

Actually, the experiments indicate that ultrashort

exposure times are a vital factor in differentiation and in suppressing undesired side reactions.

Theoretically, it would appear relatively easy to avoid undesirable side reactions, such as oxidation, by removing the air as far as possible and by irradiating either in a partial vacuum or by replacing the oxygen with inert gas; but it must be kept in mind that this can be achieved only to a limited degree, since foodstuffs per se contain so much water that the vacuum reduction cannot proceed below the evaporation point, if dehydration and subsequent changes in texture are to be avoided. Even under inert gases, the water remaining in the target would still interact with the electrons and lead to harmful changes in flavor and appearance.

To determine the over-all extent of side reactions, such as the formation of oxidation products during exposure to high-speed electrons of ultrashort duration, distilled and tap water were irradiated, and it was found that with dosages comparable to those causing complete sterilization, the hydrogen peroxide formation amounted to less than .005 per cent. These experiments were conducted at room temperature. Subsequently, we repeated the experiments with the same dosages but with progressive reduction of the temperature to -100°C ., and found a continuous decrease of hydrogen peroxide formation, the final percentage being only about 1/10 that formed at room temperature. Thus, a second method became

¹ The authors are grateful to M. P. Davidson, W. S. Wasserman, and A. A. Strelsin for making available the funds which supported these experiments. Richard Sencer has assisted considerably with the building of the radiation laboratory.

available to suppress undesired side reactions. In combination with the ultrashort exposure times, it provided the necessary means to preserve a number of raw foodstuffs, without noticeable changes in appearance, taste, and odor. Generally, it was found that the combination of these two factors suppressed not only oxidation but also all other processes, except for the most rapidly occurring chemical and biological reactions.

1/1,000,000 of a second. The law of absorption (8) and the possibility of an exact dosage are factors in favor of artificially produced electrons, which, furthermore, can be handled and directed much more easily and safely. Finally, with electrons accelerated by tensions up to 10,000,000 volts, the danger of formation of radioactive by-products in the irradiated substances is negligible, whereas the contrary is true of neutrons.

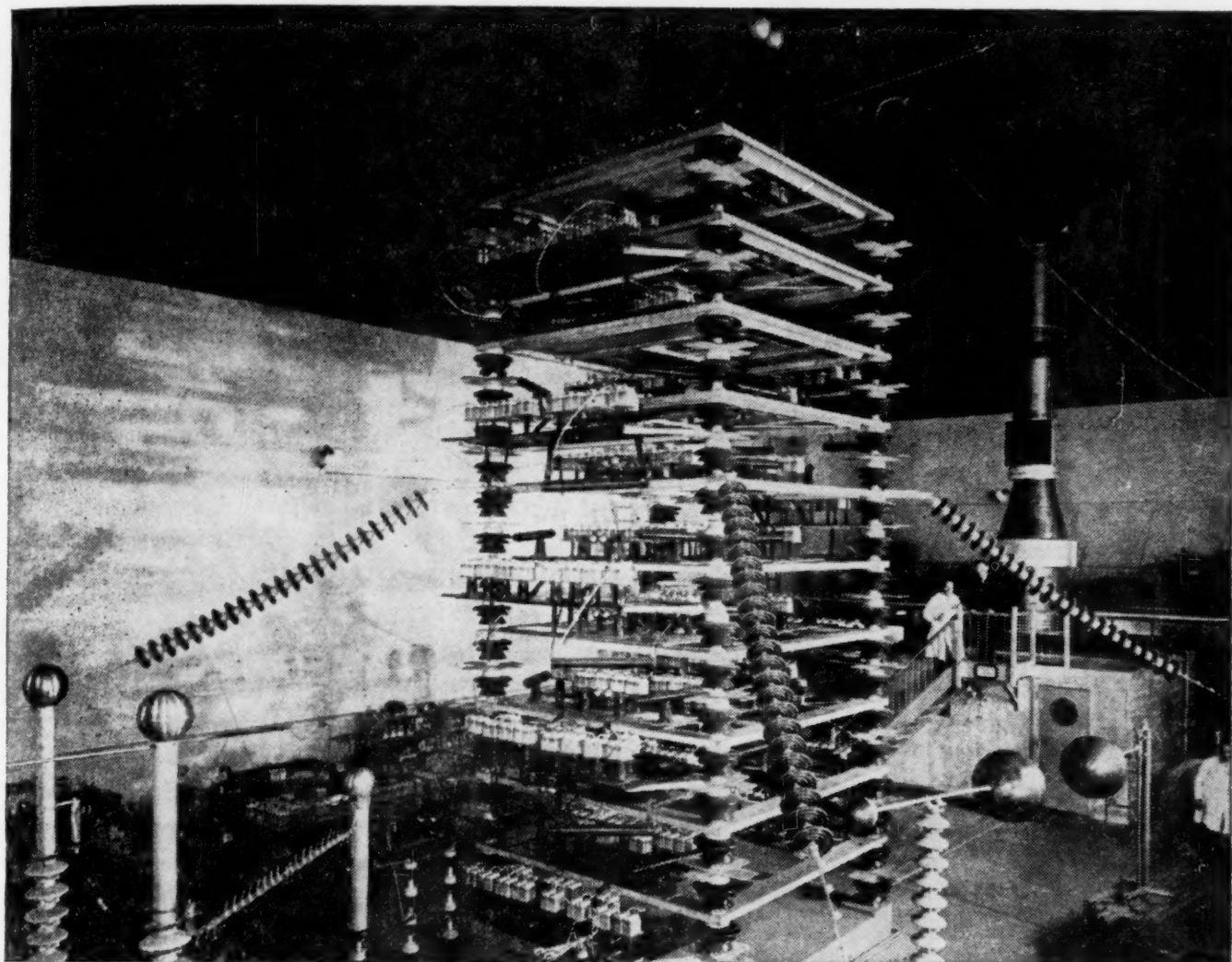


FIG. 1. The Capacitron built by Electronized Chemicals Corporation in their laboratories in Brooklyn, New York. It produces ultra-short electrical impulses of very high voltages and amperages which, in a specially designed discharge tube, are converted into correspondingly short bursts of electrons. Such bursts make it possible to bring out the true effects of radiation by suppressing certain side reactions. Therefore, the Capacitron will be used particularly in the sterilization of foodstuffs in the raw state, in the preparation of new therapeutics, and in radiation therapy.

In principle, all kinds of chemically active rays can be used under proper conditions for sterilization and preservation purposes (7), although X-rays and ultraviolet are not usable for practical purposes, for obvious reasons.

The development of the atomic pile has made available unlimited quantities of neutrons which theoretically could be used for sterilization and preservation (6). It would seem, however, that the size of the neutron and, therefore, the relatively high amount of ionization (4) exercised by each individual particle would lead to a greater amount of side reactions than would be tolerable. Furthermore, it will not be easy to construct neutron sources that operate effectively during impulses of

Moreover, highly accelerated electrons release more intensity below the surface and have an absolutely defined penetration range; thus they fulfill in an ideal way the fundamental demands of radiation therapy regarding subsurface intensity and range control.

In order to use to the fullest extent the therapeutic possibilities of highly accelerated electrons, it will be necessary often to deviate from the pattern developed in the application of hitherto used radiations such as X-rays. The biological intensity of penetrating electrons is about 500,000–1,000,000 times greater than that obtainable with X-rays. It is therefore possible to carry therapeutically sufficient amounts of radiation

through very small evacuated channels—for instance, injection needles. Thus, through such a needle can be carried enough radiation intensity for the application of therapeutic doses to diseased areas far below the surface without harming the overlying or surrounding tissues. Deep-seated cancers in rabbits were reached and eliminated by this procedure.

of a comparable density an irradiation from both sides is possible, the total penetration range thus being increased to about 24 mm. At present consideration is being given to enlarging our equipment to a practical penetration range of 70 mm., making it possible to sterilize with one impulse about 20 liters of material of the specific gravity of water. If one assumes an average

TABLE 1*

Product	No. of impulses	Original contamination	Sterility	Container	Remarks
Spore-forming G.N.B. in oil	2	25 B./cc.	Sterile	Petri dish	30-cc. sample; no morphological change
Diphtheria antitoxin	1	Unknown	"	Ampule	No loss of potency
Whole blood	1	"	"	"	No hemolysis or decrease of O ₂ uptake
Human plasma	2	"	"	"	10-cc. sample; no protein denaturation up to 12 impulses
Protein hydrolysate	2	G.N.B., GPC	"	Al. foil	10-gram sample
Novocaine solution	2	G.N.B.	"	Ampule	No chemical changes
Distilled water	3	Pyrogen	"	"	Free of pyrogen
Penicillin powder	2	Unknown	"	Al. foil	No change in potency
Brewers' yeast	3	Weevil eggs	"	" "	No change in yeast
<i>H. pertussis</i>	2	20 B./cc.	"	Petri dish	No change in antigenicity
Whole bran	2	Unknown	"	Al. foil	No change in growth-promoting properties
Trypsin	3	"	"	" "	No inactivation
Cholinesterase	2	"	"	" "	" "
Ground raw beef	2	"	"	Pliofilm bag	30-gram sample; no change in appearance
Fluid milk	1	"	"	Petri dish	50-cc. sample; no change in appearance
Pork meat patty	4	<i>S. marcescens</i>	99.9%	" "	Samples 0.6-2.5 cm. thick
Potato	4	<i>B. subtilis</i>	93.3%	" "	Samples 1.2-2.5 cm. thick

* All experiments were carried out with a 3,500,000-volt Capacitron; the impulse duration was about 1×10^{-6} second. The samples were usually irradiated within a distance of 7.5 cm. from the exit window.

We used as an electron accelerator (2) a modified impulse generator constructed according to the design first developed by E. Marx. Thereby a number of capacitor banks are charged in parallel over charging resistances and discharged in series over adjustable spark gaps. The end voltage is determined by the number of the capacitor banks as well as the charging voltage applied to each individual bank. In our installation, we used a powerful charging equipment which permits charging the condenser tower to its full capacity 50-100 times per minute. The discharge time of such an impulse generator can be varied by adjustment of the charging resistances between 10^{-4} and 10^{-7} second.

The discharge tube, immersed in a special lubricating oil, is of the laminated disc type first described by Brasch and Lange (1). Orthodox glow filament cathodes can hardly be used for our purposes, since it is necessary to handle currents of the magnitude of many thousand amperes during a split second. Therefore, a special gas cathode was developed which can be regulated within the necessary limits.

The electrons penetrate into the open through a window device, 15 cm. in diameter.

An apparatus of the above or a similar design will henceforth be referred to as a "Capacitron."

By various methods we have determined that the practical penetration range of the present Capacitron is approximately 12 mm. in water. In solid materials

discharge frequency of only 30 impulses per minute, this would be equivalent to a capacity of 600 liters per minute or 36,000 per hour, provided that the diameter of the exit device is increased to 50 mm.

So far we have been able to sterilize a wide variety of medicinals, therapeutics, and foodstuffs with penetrating electrons of ultrashort duration, as emitted from the Capacitron. The compounds, in tightly sealed containers, were either contaminated per se or had been contaminated by the addition of bacteria.

Table 1 shows some representative results of these tests. Such items as suspensions of spore-forming, gram-negative bacteria, diphtheria antitoxin, whole blood, blood plasma, protein hydrolysate, penicillin, novocaine solution, brewers' yeast, bran, proteolytic and diastatic enzymes, as well as foodstuffs such as meat, sea foods, dairy products, vegetables, and fruits, were sterilized with electrons without impairment, provided the proper conditions were used. In the case of sodium-penicillin powder, sterilization is achieved with two impulses without any detectable deterioration of potency. A similar result is obtained with brewers' yeast contaminated with weevil eggs. Whole human blood as well as human and bovine plasma were completely sterilized with one to two impulses in a distance of 10 cm. from the exit window. The whole blood showed no change in oxygen uptake, as evidenced by a Van Slyke determination, and a red cell count identical with that

of the control. Thus treated, it could be stored in closed containers over considerable periods of time without showing any noticeable changes. It is interesting, however, to note that the exposure of whole blood to excess impulses causes partial hemolysis and conversion of the hemoglobin into methemoglobin. That the sterilization of bovine plasma was not accompanied by the formation of toxic degradation products, such as peptones, was shown by injecting into a dog 50 cc. of an isotonic solution twice in an interval of six minutes without resulting change in blood pressure.

We find that the dosages necessary for sterilization have so far caused no detectable morphological changes in the microorganisms. Hence, it seems probable that bacterial death is caused by inhibitory changes in one or more of the most unstable enzyme systems essential for survival of the organism. Denaturation of structural protein is generally not detectable with electron dosages adequate to cause complete sterilization. Partial and even complete protein denaturation can, however, be achieved, the degree of denaturation depending upon the number of impulses and the stability of the native protein molecule. On the basis of these results, it seems that electrons of ultrashort duration can be adapted to serve as a satisfactory tool for the attenuation of bacteria in a graded and rigidly controllable way. Thus, it would be possible, by the change of the number of impulses as well as of the duration of the individual impulse, to reach and stabilize the various interphases between the native and the denatured state of any particular, biologically active protein. We have already been able to determine that, in the case both of diphtheria toxin and *Hemophilus pertussis*, detoxification can be obtained by exposure to high-speed electrons under suitable conditions. These examples were selected purposely, since in both cases detoxification usually is obtained by chemical means, affording a comparison of the degree of attenuation possible with electrons. Viruses are more resistant to electrons, requiring several times the dose necessary to inhibit the multiplication of most bacteria.²

Our early experiments in the field of foodstuffs demonstrated that sterilization could be achieved, although the mechanism of enzyme inhibition was then not well enough understood to obtain products which were unaltered in taste, odor, and appearance. In the meantime, we have found that the solution of this problem lies, in addition to the factors already discussed, in a rigid dosage control of the penetrating electrons, which allows selective enzyme inhibition without attacking the other constituents of the food sample. With trypsin, for example, we found that five impulses within a distance of 5 cm. from the exit window caused 16 per cent

inhibition. In this particular case, an inhibition of 92 per cent was obtained with 16 impulses. However, some enzymes of the oxydase group seem to be particularly resistant to the inactivation with accelerated, ultra-short-time electrons.³

On the basis of these and similar results on other enzyme systems we proceeded to apply electrons in graded impulses to a wide variety of meats, sea foods, dairy products, vegetables, and fruits. In general, it can be said that with impulse dosages 3-15 times the sterilization dosage, enzyme inhibition, and therefore preservation, was obtained in practically all the tested foods without any deep-going changes in the taste, odor, and appearance of the material. Although a number of these experiments are still more or less in an exploratory stage, it can already be said that a manifold increase of preservation time over the controls is possible, provided that the food samples are exposed in sealed containers and under appropriate conditions, such as the addition of an inert gas and, if necessary, cooling, during the time of the irradiation.

Table 2 shows the experimental data obtained with some representative food samples under these conditions. It will be seen that lean beef, poultry, and eggs, are the most easily preserved in the series of proteinous foods, whereas in the case of vegetables, green peas, mushrooms, and tomatoes gave satisfactory results. An irradiated steak, for instance, was unchanged for all practical purposes after storage in the incubator at 37.5° C. for 12 days. The same was true for whole eggs, as well as egg yolks and dehydrated eggs. Whole pigeon eggs, irradiated bilaterally with three impulses each, were absolutely fresh after storage for 10 weeks at room temperature. Preservation of fluid milk without changes in taste proved to be of considerable difficulty, but was finally achieved after deaeration and irradiation at low temperatures. But generally milk products and cheeses are highly susceptible to changes in taste.

Irradiation at room temperature caused changes in the red color of many of the treated food samples. In the case of meat products, the color changed frequently from red to dark purple, whereas in products such as strawberries, carrots, etc., a definite bleaching took place. We have preliminary proof that, in meat products, the change in color is due to a change in the hemoglobin similar to that occurring during the irradiation of whole blood, whereas in vegetable products, the carotenoids are changed either by oxidation or by rupture of the olefinic chain. Cooling of these foodstuffs to temperatures of -40° C. and lower during the irradiation period usually eliminated color changes without interfering with degree of sterilization and enzyme inhibition.

After exposure to high-speed electrons, sea foods such as salmon, shrimps, oysters, and lobsters were stored at elevated temperatures for periods of from 4 to

² This work is being carried out in cooperation with Dr. U. Friedemann and his associates, of the Brooklyn Jewish Hospital, Brooklyn, New York, and will be published in detail at a later date.

³ A detailed study of this problem will be the topic of a later publication.

12 days and were found to be fully satisfactory except for a slightly smoky taste, which developed after about 5 days and which may indicate the incomplete inhibition of certain very resistant enzyme systems. We would like to underscore at this point that no preservatives or antioxidants were added in any of these experiments.

A peculiar effect is the obvious sensitivity of vegetable cells to the impact of high-speed electrons. We ob-

out to illustrate this point. Highly purified olefinic monomers are known to be particularly prone to polymerization under mild conditions. Smooth polymerization of such compounds with electrons from various sources has been described repeatedly (3). On exposure of such representative compounds as propylene, isobutylene, vinylacetate, and styrene, at room temperature, to electron impulses of extremely short duration,

TABLE 2*†

Raw foodstuffs	No. of impulses	Storage temperature (°C.)	Storage time (days)	Appearance	Taste‡	Odor	Notes
<i>Animal origin:</i>							
Lean beef.....	8	37.5	12	Good	Good	Good	Tenderized; purple color
Ground pork.....	8	"	6	"	"	"	Purple color
Calves' liver.....	6	"	5	Fair	"	"	Brownish color
Chicken breast.....	8	27	12	Good	"	"	
Chicken liver.....	6	"	7	"	Fair	"	Slightly bitter taste; discoloration
Chicken heart.....	8	"	7	"	Good	Fair	Slightly stale odor
Oyster.....	6	37.5	5	"	Fair	Good	Slightly cooked and rancid taste
Salmon.....	14	"	12	"	"	"	Slightly cooked taste
Shrimp.....	12	"	8	"	Good	"	
Lobster.....	10	26	10	"	"	"	No change in color
Whole pigeon egg.....	12	27	49	"	"	"	
Egg yolk (chicken).....	6	28	12	"	"	"	
Fluid milk.....	6	37.5	6	"	"	"	Vacuum deaerated with nitrogen; cooled to -30°C.
Fluid cream.....	8	"	6	"	"	Fair	{ Heavy offtaste unless irradiated under special conditions
Powdered cream.....	6	"	20	"	"	"	
Cream cheese.....	12	26	12	"	"	"	
<i>Plant origin:</i>							
Tomato, sliced.....	10	27	10	Fair	"	Good	Texture slightly mushy
Peas.....	12	27	16	Good	Fair	"	Some loss of flavor
Carrots.....	14	37.5	10	Fair	Good	"	Texture good, but bleached
Mushrooms.....	8	"	10	"	"	"	Brown discoloration
Asparagus.....	12	27	8	Good	Fair	"	Sour taste
Apple, sliced.....	10	25	13	Fair	Good	"	Soft texture
Pear, sliced.....	10	"	"	Poor	"	"	Poor texture
Peach, sliced.....	8	"	8	Fair	"	"	Soft texture; some discoloration
Strawberry, whole.....	12	28	10	Good	"	"	Irradiation at -30°C.; irradiation at room temperature causes bleaching
Grapes, whole.....	14	37.5	12	"	"	"	
Cherries, whole.....	16	28	14	"	"	"	
Blueberries, whole.....	8	34	8	"	"	"	
Pineapple, sliced.....	10	28	8	"	Fair	"	Slightly sour
Orange, sliced.....	10	28	8	"	"	"	

* All experiments were carried out with a 3,500,000-volt Capacitron. The impulse duration was about 1×10^{-6} second. The samples were about 0.6-1.2 cm. thick and not more than 12.5 cm. in diameter.

† All controls were handled in exactly the same manner as the irradiated samples. Changes in appearance, taste, or odor were manifest in all instances during the first 4-18 hours of storage.

‡ The taste tests were performed either on the raw material or, in some cases, both on the raw and the cooked samples.

served repeatedly that irradiation with overdoses of electrons caused partial destruction of the cell walls, combined with a structural breakdown and an oozing out of the cell contents. This is particularly noticeable with fruit slices such as apples, pears, and strawberries, while whole fruits such as grapes, blueberries, and cherries were considerably more stable. This effect may be explained by the less pronounced elasticity of the plant cell as compared to the animal cell.

In order to emphasize further the distinct difference between impulse irradiation of extremely short duration and continuous or semicontinuous irradiation, we submit a few of many chemical experiments that were carried

we found that no significant degree of polymerization was detectable, although the kinetic energy which had been released was many times in excess of the amount required to start the chain reaction. The number of impulses used in these experiments varied from 3 to 25, the samples (10 grams each) being within a distance of 4 cm. from the exit window. Similarly, the drying and the polymerization effect of ultraviolet on vegetable oils (7) such as linseed, castor, and cotton-seed oil cannot be duplicated by even extended exposures to high-speed electrons. Viscosity, specific gravity, and iodine number remain unchanged after exposures up to 20 impulses at room temperature.

It is quite remarkable that, with a time element of too short a duration for the initiation of a reaction, there also seems to be no accumulation factor for many chemical compounds.

Many phenomena which have been attributed to the action of radiation proper represent in reality merely the cumulative effect of rays together with nonspecific, radiation-caused, side reactions. The latter include elevation of temperature, oxidative processes on the surface—and within the target—as well as a multitude of other chemical reactions. In consequence, the suppression of by-effects will illustrate automatically what may be called “the pure radiation principle” and will facilitate the more intimate understanding of the fundamentals involved. The Capacitron carries sufficient intensities into the targets in such short times that most chemical reactions can be eliminated while the effective biological impact is maintained. Therefore, a detailed study from this specific angle seems to be indicated, and for principal reasons an even further shortening of the exposure time to about 10^{-8} second must be considered.

Although a great deal of exploratory and developmental work is yet to be done, there can be no doubt that a process which, among other things, permits pres-

ervation in a raw state and causes chemical and biological effects of such a highly differentiated nature, will be found useful in many applications beyond those reported here. An important consideration, for practical purposes, will be whether or not the operating costs of such a device are prohibitive. Detailed estimates show that such expenditures will not materially increase the final price of the treated product, provided that the output of the Capacitron is adapted to the desired purpose.

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NEWS and Notes

A meeting of the Inter-Society Committee for a National Science Foundation has been called for 10:00 A.M., Sunday, February 23, in Washington at Hotel 2400 by Kirtley F. Mather, who is chairman of the Council Committee arranging for the organization. Since the Boston meeting, at which a resolution calling for this action was adopted, invitations have been extended to a large number of national scientific and educational groups asking for the appointment of delegates to the Washington meeting. The response was immediate, so that some 60 delegates are now receiving instruction from their group.

About People

Wendell M. Stanley, Rockefeller Institute for Medical Research, Princeton, New Jersey, and 1946 Nobel Prize winner in chemistry, addressed the Detroit Section of the American Chemical Society January 15 on the subject of influenza vaccines. Vaccine separated from chick

embryonic fluid by centrifuging, Dr. Stanley said, consists almost exclusively of purified virus, while other types, prepared by elution, alternate freezing and thawing, or precipitation with chemicals, include as impurities as much as 80 per cent of chick proteins and other material containing nitrogen. Carl F. Graham, Research Department, Wyandotte Chemicals Corporation, chairman of the Section, presided at the meeting.

William Walter Greulich, professor of anatomy, Stanford University School of Medicine, and director of the Brush Foundation, has returned to the United States after three months in Australia and New Zealand, where he visited universities and medical schools and lectured to chapters of the British Medical Association in all principal cities of the two countries.

Saul B. Arenson has been made professor emeritus of inorganic chemistry at the University of Cincinnati. Since August 1946, he has been convalescing from a heart attack at 1884 Laurel Canyon Boulevard, Los Angeles 46, California.

W. S. Flory, Jr. has been appointed professor of experimental horticulture and vice-director of the Blandy Experimental Farm, University of Virginia. His new work, effective February 1, follows service

as horticulturist of the Virginia Agricultural Experiment Station.

Percy Williams Bridgman, 1946 Nobel Prize winner for work in physics, was honored at a dinner given in Boston January 11 by Dean of the Faculty of Arts and Sciences Paul H. Buck, Harvard University. Speakers were I. I. Rabi, Columbia University, who received the Nobel award in physics in 1944; Theodore Lyman, director, Jefferson Physical Laboratory, Harvard; John Clarke Slater, chairman, Physics Department, Massachusetts Institute of Technology; and James B. Conant, president of Harvard. Guests included George R. Minot and William P. Murphy, Harvard Medical School, who won the prize in physiology and medicine in 1934; Manuel S. Vallarta, Mexican physicist and representative on the U. N. Atomic Energy Commission; A. W. Hull, General Electric Company; Harvey N. Davis, president, Stevens Institute of Technology; George A. Campbell, telephone research engineer of Upper Montclair, New Jersey; Gordon F. Hull, Dartmouth College; and Karl K. Darrow, Columbia University.

Sven Wingquist, inventor of the spherical ball bearing and founder of the SKF ball-bearing industry, on December 10 celebrated his 70th birthday by donat-

ing his estate, Remningstorp, in South Sweden, to a foundation for forest research. The estate, comprising about 3,700 acres and valued at \$278,000, is heavily forested. Activities will be carried on in collaboration with the Swedish State Forest Research Institute.

Helen Louise Ellis, Wilson College, has joined the research staff of the Smith, Kline & French Laboratories, Philadelphia.

Oskar Baudisch, research director, Saratoga Springs Commission, will address a meeting of the Biochemical Society, University of Stockholm, Sweden, and the Polish Chemical Society and University of Poznań, Poland, in February.

Laurence H. Snyder, chairman, Department of Zoology and Entomology, Ohio State University, will address a joint meeting of Phi Beta Kappa and Sigma Xi at Rutgers University, February 17, on human and medical genetics. He presented lectures on this subject before the Cayuga County Medical Society December 5, at Wells College December 6, and before the Northwestern University chapter of Sigma Xi January 10.

Visitors From Abroad

N. R. Dhar, head, Chemistry Department, University of Allahabad, India, will visit the United States in June and be available to lecture at universities on biochemistry. He has carried on work in physical chemistry in the field of colloidal gels, aging and oxidation processes, and allied subjects. Further information about lectures may be obtained from Thomas S. Gardner, Scientific Department, Hoffmann-La Roche, Inc., Nutley, New Jersey, with whom Prof. Dhar has communicated.

Grants and Awards

The Medal of Merit was presented by the Navy December 27 to Philip McCord Morse, director of Brookhaven National Laboratory, for service as wartime director of the Anti-Submarine Warfare Research Group in the Atlantic. Dr. Morse is on leave as professor of physics from M.I.T.

Clarence S. Ross, chief, Petrology Section, Geological Survey, was awarded the Roebling Medal for achievement in mineral research January 3 by the Min-

eralogical Society of America at its annual meeting in Chicago. Dr. Ross, who has been on the staff of the Survey since 1917, received the Orton Award for research in ceramic minerals from the American Ceramics Society in 1945.

Walter R. Kirner, director, Chemical-Biological Coordination Center, NRC, Washington, D. C., was recently awarded the Medal of Merit. He was employed by the National Defense Research Committee from 1940 to 1946 and served as chief of the Chemistry Division from 1942 to 1946. During 1943-44 he was also chief, Chemical Research Branch, Technical Division, Office of the Chief of the Chemical Warfare Service.

Bureau of Ordnance Development Awards have recently been received by W. E. Kappauf, Department of Psychology, Princeton University; Franklin V. Taylor, Psychology Section, Naval Research Laboratory; Alston S. Householder, Monsanto Chemical Company, Oak Ridge, Tennessee; Thomas G. Hermans, Department of Psychology, University of Washington, Seattle; and Henry P. Birmingham, Naval Research Laboratory. The awards were made on December 20 in recognition of work on lead-computing gun sights in connection with NDRC Project N-111.

Elmer D. Merrill, Arnold professor of botany, Arnold Arboretum, Harvard University, was awarded the George Robert White Medal of Honor by the Massachusetts Horticultural Society January 8, as the person who "in recent years has done most to advance the interest of horticulture in its broadest sense." Dr. Merrill has also been appointed honorary collaborator, Botanical Garden, Buitenzorg, Java, in appreciation of his work on the flora of Malaysia over a period of 44 years.

M. L. Crossley, director of research, American Cyanamid Company, will receive the 1947 gold medal of the American Institute of Chemists at its annual meeting in May. Foster D. Snell, president of the Institute, stated that the award is in recognition not only of Dr. Crossley's work with dyes and pharmaceuticals, but also his activities in behalf of the profession of chemist. Dr. Crossley has conducted research on the relation of molecular structure to color in organic compounds; on synthesis of dyes; on discovery and industrial development

of the sulfa drugs; and on the chemistry of infectious diseases. Among previous recipients of the medal have been Lafayette B. Mendel, Yale University; James B. Conant, Harvard University; Marston T. Bogert, Columbia University; and last year, Robert P. Russell, Standard Oil Development Company.

Franz Weidenreich, American Museum of Natural History, on December 28 was awarded the Viking Fund Medal and prize of \$1,000 in physical anthropology. The newly created award, presented at the annual meeting of the American Association of Physical Anthropologists, cited Dr. Weidenreich for his many contributions to paleoanthropology and especially recent studies on fossil man in China and Java.

The Morrison Award of the American Society of Animal Production was granted J. L. Lush, professor of animal breeding, Iowa State College, at the annual meeting of the Society November 30. The award of \$1,000, first of five to be made from funds provided by F. B. Morrison, Cornell University, and his wife, Elsie B. Morrison, is given to members of the Society who have done "outstanding recent research of direct importance to livestock production."

Alfred V. Kidder, Harvard archaeologist, has been awarded the Viking Fund Prize and Medal in archaeology for 1946. The prize of \$1,000 and a gold medal, provided by the Viking Fund, is awarded annually by the Society for American Archaeology to the person considered to have made the outstanding contribution to archaeology.

Colleges and Universities

Cambridge University, England, has announced that elections will be held this month to the professorship of astrophysics, which will fall vacant in October 1947, on retirement of Prof. F. J. M. Stratton.

Lehigh University will conduct research on thermal and electrical properties of aluminum and its alloys under a grant by the Aluminum Company of America. The study will be under the direction of Charles C. Bidwell, professor of physics.

Northwestern University has just begun a \$500,000 three-year research program on communication devices, financed by the Navy and directed by Walter S.

Huxford and Robert J. Cashman, professors of physics, Northwestern Technological Institute. The program is an extension of wartime research which developed a new invisible-ray telephone and new types of photoelectric cells used in the telephone and various secret weapons. The telephone, which transmits the voice on invisible rays of infrared light, was used during the war for short-range, ship-to-ship communication and may find first peacetime application in crowded harbors and airports where radio wave bands are jammed.

The Ohio State University has announced appointment of Alpheus W. Smith, technical counselor and administrator, and Max Astrachen, associate professor, Wright Field Graduate Center. Dr. Smith retired as dean of the Graduate School and chairman of the Department of Physics last year after 37 years service at Ohio State.

The University also appointed Clifford R. Cutright, Claude R. Neiswander, and Ralph B. Neiswander, associate professors of zoology and entomology; Earle R. Caley, associate professor of chemistry; W. P. Judkins, assistant professor of horticulture and forestry; and Robert B. Jacques, assistant professor of electrical engineering.

Approval has been given to creation of a Department of Radiology in the College of Medicine, effective July 1, 1947, as recommended by the faculty council.

Industrial Laboratories

Wm. S. Merrell Company announces the appointment of Frederic E. Shaffer, University of Louisville, to the pharmacology division of its research department.

The Eastman Kodak Company Research Laboratories has had in operation for several months an apparatus for the separation of C^{13} by the chemical exchange reaction developed by H. C. Urey. Operation has reached a point where it is possible for the Laboratories to make the first commercial shipment of C^{13} in the 20-25 per cent concentration range. Initial production is on a small scale, but larger fractionating columns have been installed and will soon be in operation.

The Eastman Kodak Company has agreed to supply essentially its entire initial production to the National Re-

search Council's Committee on Growth.

A tentative price schedule has been established for material produced in the present small-scale apparatus. Prices range from \$100 per gram of excess C^{13} in the 3-5 per cent range, to \$250 in the 16.1-18.0 per cent range, and \$400 at 23.1-26.0 per cent. Initially, the C^{13} will be available as potassium cyanide, although it is expected synthetic organic compounds containing C^{13} will ultimately be available. Among the first of these will be methanol.

The tracer carbon, C^{13} , is an addition to the nitrogen isotope concentrates previously produced in the Eastman Research Laboratories. The N^{15} is regularly available in concentrations of 14, 30, and 60 atom per cent, at prices of \$150, \$200, and \$300 per gram of N^{15} , respectively. Inquiries concerning C^{13} or N^{15} should be addressed to Eastman Kodak Company, Research Laboratory, Dept. WOK, Kodak Park Works, Rochester 4, New York.

Meetings

The Chemical Society, London, now arranging for the celebration of its centenary in London in July 1947, is planning an exhibition in the Science Museum illustrating the development of British chemistry during the past 100 years.

The American Society of Mechanical Engineers has announced the following schedule of 1947 meetings: Spring Meeting, Tulsa, Oklahoma, March 2-5; Oil and Gas Power 19th National Conference, Cleveland, Ohio, May 21-24; Aviation Meeting, Los Angeles, California, May 26-29; Wood Industries National Conference, Madison, Wisconsin, June 12-13; Semiannual Meeting, Chicago, Illinois, June 16-19; Applied Mechanics 13th National Conference, June, time and place not set; Fall Meeting, Salt Lake City, Utah, September 1-4; Industrial Instruments and Regulators Division, Chicago, time not set; Petroleum Mechanical Engineering Conference, Houston, Texas, October 6-8; Fuels Division Meeting with Coal Division, American Institute of Mining and Metallurgical Engineers, Cincinnati, Ohio, time not set; Annual Meeting, New York City or Atlantic City, New Jersey, December 2-5.

The 11th International Congress of Pure and Applied Chemistry will be

held in London July 17-24 at the time of centenary celebrations of the Chemical Society in London. At the 10th International Congress in Rome, 1938, the 11th Congress was scheduled for London, 1941, with centenary celebrations of the Chemical Society, but when war broke out, both events were postponed. Centenary meetings will be July 15-17, immediately before the Congress.

The Eastern Association of Electroencephalographers will hold a three-day meeting at the Montreal Neurological Institute, 3801 University Street, Montreal, February 21-23.

The 17th International Physiological Congress, originally scheduled for 1941, will be held at Oxford, England, July 21-25, 1947. Due to a shortage of living accommodations, the British Committee has issued invitations in the first instance only to physiologists who are themselves members of the physiological societies of their own countries, a letter from E. G. T. Liddell, of Oxford, states. Nonetheless, the Congress Committee has authorized the American Physiological Society to accept an additional 500 requests for invitations, according to Wallace O. Fenn, president of the Society. Applications from members will be accepted in order of their receipt and will be given priority over applications from nonmembers. In the case of nonmembers, priority will be given to the physiological qualifications and interests of applicants. Persons who wish to attend may communicate with the secretary of the Society, Maurice B. Visscher, University of Minnesota, Minneapolis, prior to February 28.

Elections

The American Association of Physical Anthropologists, meeting in Chicago December 28, re-elected Wilton M. Krogman, University of Chicago, president. The Association also elected Gabriel W. Lasker, Wayne University, secretary-treasurer; Carleton S. Coon, Harvard University, to the executive committee; and Joseph B. Birdsall, Harvard University, an assistant editor.

The American Society of Electroencephalography, meeting for the first time in Boston in December 1946, to "supervise and raise the standards of laboratories, workers, and publications

in this field," elected the following officers: Herbert Jasper and Frederick A. Gibbs, American Physiological Society, president and vice-president, respectively; Robert S. Schwab, American Psychiatric Association, secretary; and Mary A. B. Brazier, treasurer. The council of seven members, which formed the new society, consisted of Robert Aird and Charles Aring, American Neurological Association, Charles Stephenson, American Psychiatric Association, and E. J. Baldes, American Medical Association, in addition to Drs. Jasper, Gibbs, and Schwab.

Recent Deaths

Henry G. Avers, 61, a chief mathematician with the U. S. Coast and Geodetic Survey since 1924, died at his home in Washington January 19.

Clarence Martin Jackson, 71, head, Department of Anatomy, University of Minnesota, 1913-41, died in Minneapolis January 17.

The Tissue Culture Commission, a new informal organization of investigators who use the techniques of tissue culture, at its first meeting, held recently, elected the following temporary committee: Keith R. Porter, chairman; Margaret R. Murray, secretary; George O. Gey, Duncan C. Hetherington, and Charles M. Pomerat, executive members; Honor B. Fell, European member-at-large.

Initial aims of the Commission are to examine the possibility of preparing chicken plasma, placental cord serum, horse serum, serum ultrafiltrate, buffered saline solutions, and embryo extract centrally for distribution at moderate cost, and to prepare a bibliography of the published research in tissue culture.

Anyone using the tissue culture method is eligible for membership in the Commission, and inquiries may be addressed to Margaret R. Murray, College of Physicians and Surgeons, New York 32, New York.

The National Registry of Rare Chemicals, Armour Research Foundation, 35 West 33rd Street, Chicago, lists the following wanted chemicals: arterenol; nucleoproteins; β -(m-hydroxyphenyl)-ethylamine; trimethyl bismuth; trimethyl arsenic; trimethyl antimony; quinuclidine; 2-pyridine aldehyde; 3-pyridine al-

dehyde; 2,3,4-trimethylbenzaldehyde; 1-phenylalanine; N-piperidinoacetaldehyde; thebaine; p-benzylphenol; divinyl sulfide; divinyl disulfide; alkannin; piperidinomethyl-1,4-benzodioxan (933F); 2-diethylaminoethyl-1,4-benzodioxan (883F); 2-phenylbenzopyrone; and di-*o*-tolylzinc.

"Prevention of Deterioration Abstracts," including journal articles, patents, specifications, unpublished reports by Army, Navy, and other governmental groups, and unpublished British, Australian, and Canadian reports, are now available on a yearly subscription basis. The price, including a binder and index guides, will be \$35 for the fiscal year July 1-June 30, back issues being supplied since the Abstracts started in April 1946. There will be about 1,500 pages of Abstracts a year, in loose-leaf form so they may be arranged as desired. All pages under any one heading will be numbered consecutively.

Abstracts are set up under the following headings: electrical and electronic equipment; finished assemblies; fungicides; lacquers, paints, and varnishes; leather; lubricants; metals; microorganisms; optical instruments; packaging; paper; plastics, resins, rubbers, and waxes; storage; textiles; and wood. Subscriptions may be obtained from Prevention of Deterioration Center, Room 204, 2101 Constitution Avenue, Washington, D. C.

The British Glaciological Society, founded in 1945, has issued in 1947 the first number of *The Journal of Glaciology*, designed to publish not only scientific transactions of the Society, but discussions of problems relating to snow and ice in all modes of occurrence. The journal is expected to fill a need in view of growing interest in polar and circum-polar regions and improved aerial navigation and oversnow travel, and especially because *Zeitschrift für Gletscherkunde*, in past years the only glaciological magazine, was discontinued during the war and has not yet been revived.

The editorial committee is headed by Gerald Seligman, under whose leadership the Society was originally organized in 1936 as the Association for the Study of Snow and Ice. Offices are at the Royal Geographical Society, Kensington Gore, London, S. W. 7.

Present officers of the British Glacio-

logical Society are Gerald Seligman, president; J. M. Wordie, vice-president; and an executive committee of nine members.

An International Conference on High Polymers was held at the University in Strasbourg the week of November 25, first of a number of conferences on special subjects to be held in France, arranged by the Centre National de Recherche Scientifique and under sponsorship of the Rockefeller Foundation. The papers, which were restricted to the subject of molecular properties of large molecules, will appear in an early issue of the *Journal de Chimie Physique*. Members of the conference were generally agreed on desirability of a permanent international organization for surveying the study of macromolecules and an international journal containing articles of general importance in more than one language. Interested people are asked to write M. L. Huggins, Kodak Research Laboratories, Rochester, New York, or Charles Sadron, Institut de Physique, 3, rue de l'Université, Strasbourg.

German physicists of the British zone of occupation held meetings at Göttingen October 4-6 and formed a German Physical Society for the British Zone, with Max von Laue, Göttingen, chairman, and a board of five members each for the sections Hannover-Braunschweig and Rheinland. All former members of the Deutsche Physikalische Gesellschaft now resident in the zone will automatically be accepted as members of the new organization and others may apply for membership. About 300 physicists were present and 17 papers read. A few visitors from the American and Soviet zones of occupation attended as well as representatives of the British Control Commission and physicists from Britain. Statutes and bylaws of the society are still subject to approval by the British Military Government.

Japanese physicians are in need of American scientific books, according to Lt. Col. Warner F. Bowers, surgical consultant for the Pacific theater, who visits all American hospitals in Japan as well as Japanese hospitals connected with the Imperial Japanese University Medical Schools. Since the Japanese language does not contain technical terms used in clinical surgery, German books have been used and German records kept. Although

there seems to be a desire to change terminology and records to English, most scientists are not sufficiently familiar with English to make the change. Hence, Lt. Col. Bowers avers, textbooks in English dealing with surgery and the basic sciences are needed, and since Japanese doctors cannot order from America, he suggests donation of books. Packages up to 11 pounds can be sent direct and may be mailed to Kikuo Ohtsuki or Kentary Shimizu, Department of Surgery, Tokyo Imperial University Medical School, Tokyo, Japan.

U. S. relations with scientific laboratories in other countries have been substantially renewed since the end of the war, according to the December *Technical News Bulletin*, of the National Bureau of Standards.

During the summer of 1946, 12 members of the Bureau visited other nations, 18 Bureau engineers were and still are at various stations in the Pacific, and another engineer was recalled by the Army to aid in organizing a Standards Bureau in Korea.

In the six months, May 1–November 1, 176 representatives of 35 countries visited the Bureau. Included were 10 directors of research institutions with programs as broad as the Bureau's and 9 directors of specialized research institutions, as well as research engineers, university professors, government officials, industrialists, and laboratory workers.

Bureau scientists report that European science is recovering rapidly from the war, national encouragement of science is widely discussed, military restrictions on interchange are being removed, and there seems to be a sincere desire to promote international good will on the part of scientists.

The Royal Society, London, has elected C. J. Mackenzie, president, National Research Council of Canada, a Fellow of the Society under the statute providing for election of persons who "have rendered conspicuous service to the cause of science or are such that their election would be of signal benefit to the Society."

Two Royal Medals for 1946 were awarded by the Society to Sir Lawrence Bragg, O.B.E., F.R.S., for researches in the sciences of X-ray structure analysis and X-ray spectroscopy, and C. D. Darlington, F.R.S., for researches in cytology and genetics.

The following awards of medals were also made: the Copley Medal to E. D. Adrian, O.M., F.R.S., for researches on the fundamental nature of nervous activity, and recently on localization of certain nervous functions; the Rumford Medal to Sir Alfred Egerton, F.R.S., for his part in the application of modern physical chemistry to many technological problems; the Davy Medal to C. K. Ingold, F.R.S., for work in applying physical methods to problems in organic chemistry; the Darwin Medal to Sir D'Arcy Thompson, C.B., F.R.S., for contributions to the development of biology; the Sylvester Medal to G. N. Watson, F.R.S., for contributions to pure mathematics in the field of mathematical analysis and in particular for work on asymptotic expansion and general transforms; and the Hughes Medal to J. T. Randall, F.R.S., for researches into fluorescent materials and production of high-frequency electromagnetic radiation.

The National Science Teachers Association's Year Book for 1946, *Time for Science Instruction*, recently appeared under the editorship of Dwight E. Solberger, State Teachers College, Indiana, Pennsylvania. Consisting of 13 articles, the Year Book, is chiefly concerned with 1) the tendency to give science less time in weekly schedules of students, and 2) need for more time than mere textbook instruction due to handling equipment, experimentation, and field trips. Copies may be obtained for \$.50 from National Science Teachers Association, 1201 16th Street, N.W., Washington, D. C.

The National Geographic Society presented Matthew W. Stirling and Mrs. Stirling at a general session on Saturday afternoon, December 28, at the AAAS Boston meetings. The program consisted of a report in nontechnical language, illustrated by colored motion pictures, of eight expeditions made by the Stirlings under the auspices of the National Geographic Society and the Smithsonian Institution. Dr. and Mrs. Stirling were introduced to a capacity audience in Symphony Hall by Charles F. Kettering, president of AAAS for 1946, and life trustee of the National Geographic Society.

Optical and mechanical work on the 200-inch telescope on Palomar Mountain has been resumed since the

war, and it is expected to be in operation in the summer of 1947, according to the 1946 report of the president, Carnegie Institution of Washington.

The California Institute of Technology and the Carnegie Institution of Washington have approved plans for unitary operation of the scientific program of the Observatory on Palomar Mountain and Mount Wilson Observatory by graduate training at the Institute under an astrophysics staff of Institution as well as Institute staff members. A committee, headed by E. P. Hubble, Mount Wilson Observatory, has been appointed to formulate a broad and long-term program of research for the combined observatories.

Walter S. Adams, who retired January 1, 1946, after more than 40 years service at Mount Wilson Observatory, has continued with the Observatory as research associate and has been active in arrangements preliminary to joint operation of the two observatories, announced soon after his retirement.

Activities of the Psychiatric Personnel Placement Service, operated jointly for the past year by the American Psychiatric Association and the National Committee for Mental Hygiene, have been transferred to the latter organization. Applications from physicians seeking placement in psychiatry should be directed to the National Committee for Mental Hygiene, 1790 Broadway, New York 19, New York, which has a complete file of positions and training opportunities in psychiatry, obtained through nationwide surveys of general and state hospitals, private mental hospitals, community and mental hygiene clinics, medical schools, and foundations.

Commonwealth Fund

By far the greater part of the \$2,121,917 appropriated by The Commonwealth Fund during the year ended September 30, 1946 went to promote and maintain health, the Fund's 1946 annual report points out. Distribution of funds was as follows: Division of Education, \$149,819; Division of Rural Hospitals, \$581,567; and under special grants, Division of Public Health, \$278,194; Mental Health, \$294,040; Medical Research, \$447,391; Medical Education, \$224,850; Miscellaneous, \$76,100.

While divisions are kept separate for

budgetary convenience, the report states, the most interesting work of the year was done in areas where they overlap. Nothing in the Fund's year, the report goes on, was more rewarding than its collaboration with several young psychiatrists in the pilot course in psychotherapy for general physicians offered at the University of Minnesota last April. The course, which spearheaded the Fund's mental hygiene program, "was an attempt, on a small scale to get the most pertinent parts of basic psychiatric thinking into general medicine, which with this reinforcement may become the center around which medicine and its specialties are reintegrated."

Lectures dealt with the personality, its development, and its disorders; interplay of the emotions and physical function; physician-patient relationship; and elements of psychotherapy, the report shows. An experiment in adapting similar instruction to postgraduate extension programs is being made with the Fund's help in Tennessee.

Commonwealth Fund Fellowships were re-established last year, and in the fall 20 British students arrived in the United States for study at various universities, 13 of the 20 being in the sciences. Between 1925 and 1941, when the fellowships were suspended, 411 Fellows visited this country as guests of the Fund for advanced study, it was shown, but with resumption of British fellowships the wartime program of fellowship aid to physicians and public health workers from the Latin-American countries was terminated. For the year 1946-47 only four appointments were made.

Seven of the eight new books published by the Fund in 1946 were studies sponsored by the Committee on Medicine and the Changing Order of the New York Academy of Medicine, designed "to provide the framework for an understanding of the current medical situation and its trends," the report states. In addition to these books, a handbook and two pamphlets for free distribution appeared during the year.

NRC News

A Chemical-Biological Coordination Center with headquarters in Washington, D. C., has been organized, funds for its operation being provided by the War Department, Navy Department, and American Cancer Society.

Primary functions of this Center are to:

(1) Collect and assemble information concerning the relation of chemical structure to biological activity. In addition to the mass of information scattered throughout the literature a great deal of work on this subject was carried out during the war, the results of which are still unpublished and should be organized so as to be available to those interested. To facilitate handling these data the Center has been actively developing chemical and biological coding systems so that chemical and biological data can be placed on punch cards and sorted by means of machines. In this way a vast number of facts concerning the chemical structure, physical characteristics, and biological actions of each compound can be quickly ascertained. This constitutes an important advance in the recording and utilization of scientific information.

(2) Sponsor the preliminary testing or "screening" of compounds on a variety of plants and animals to determine biological effects of the compounds. Such tests should serve to uncover leads for further research which may result in the practical use of the compounds.

The results of these tests will also be incorporated into the files of the Center. These files, including information concerning the relation of chemical structure and biological activity and results of the screening tests, will be available not only to sponsoring agencies but to scientists generally upon request.

A preliminary survey indicates that both old and newly synthesized compounds will be received in adequate numbers from university and industrial laboratories.

For the immediate future particular attention will be directed toward disclosure of compounds that may be useful for control of insects and rodents, diseases of animals, as well as plants, caused by microbiological agents, and also for the control of malignancies. The following agencies are cooperating in the screening program: Bureau of Entomology and Plant Quarantine, U. S. Department of Agriculture; Chemical Corps—Biological Division; Chemical Corps—Medical Division; Fish and Wildlife Service, U. S. Department of Interior; National Cancer Institute, U. S. Public Health Service; National Institute of Health, U. S. Public Health Service; Prevention of Deterioration Center, National Research Council; and Sloan-Kettering Institute for Cancer Research, American Cancer Society.

W. R. Kirner, formerly chief of Division 9, NDRC, is director of the Center. An advisory committee, under chairmanship of M. C. Winternitz, consists of the following scientists representing the fields indicated: Roger Adams, organic chemistry; W. A. Noyes, physical chemistry; J. S. Fruton, biochemistry; J. H. Mueller, microbiology; R. B. Friend, entomology; Remington Kellogg, mammalogy; McKee Cattell, physiology and pharmacology; M. C. Winternitz, pathology; W. T. Longcope, medicine; Harry Eagle, chemotherapy; C. P. Rhoads, malignancy; Abel Wolman, sanitary engineering; R. A. Kelser, veterinary medicine; and R. F. Griggs, plant ecology.

A Pacific Science Board, recently appointed by the Chairman of the Council, is composed of the following scientists: Knowles A. Ryerson, College of Agriculture, University of California, chairman; Beno Gutenberg, California Institute of Technology; Ross G. Harrison, Yale University; Remington Kellogg, U. S. National Museum; Elmer D. Merrill, Harvard University; George P. Murdock, Yale University; Robert Cushman Murphy, American Museum of Natural History; Thomas M. Rivers, Rockefeller Institute for Medical Research; Harald U. Sverdrup, University of California; and Harold J. Coolidge, Harvard University, executive secretary (ex officio).

This Board, which maintains an office in the NRC building, Washington, D. C., has been established to aid scientists of America who wish to engage in scientific investigations for which there is a need in the Pacific area, advise governmental and other agencies on scientific matters pertaining to the Pacific, and further international cooperation in the field of Pacific science.

Applications to the Committee for Research in Problems of Sex for financial aid during the year beginning July 1, for work on fundamental problems of sex and reproduction, should be received by Dr. Robert M. Yerkes, Yale School of Medicine, New Haven 11, Connecticut, not later than April 1. Although hormonal investigations continue to command the interest and support of the Committee, in accordance with current policy preference will ordinarily be given to proposals for the investigation of neurological, psychobiological, and behavioral problems of sex and reproduction.

TECHNICAL PAPERS

Differences¹ in Physiological Activity in Brown and White Fat as Revealed by Histochemical Reactions¹

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Since the discovery by Hoffmann and Wertheimer (5) that fat consumes oxygen, subsequent investigations have disclosed that adipose tissue possesses a number of biochemical activities not previously suspected. Recent experiments by Schoenheimer (7), using isotopic compounds as markers, have shown that lipids of the fat depots are not static reserves but are constantly subject to a variety of highly complex chemical reactions of synthesis, degradation, and interconversion. These findings have stimulated renewed interest in the biochemistry and histology of this tissue, so long regarded as metabolically inert. In addition to the white or yellow adipose tissue which occurs in all mammals, many species possess gland-like masses of so-called brown fat in the interscapular, axillary, and inguinal regions. The function of brown adipose tissue is obscure, but evidence is accumulating which suggests that it is quite different from that of white fat. It is known to consume more oxygen than white fat (1). Indeed, computed as fat-free tissue, its respiration is as great as that of kidney, and it is as active in oxidizing succinate and pyruvate. It contains cytochrome C and cytochrome oxidase and is rich in ascorbic acid and diphosphothiamine, according to Hook and Barron (6). We have been interested in comparing the two types of fat with regard to their histochemical reactions for glycogen and lipase.

Glycogen is not found in the adipose tissues of rats in a normal nutritional state. It can, however, be demonstrated in the fat cells of animals being refed with carbohydrate after a period of fasting (2). We have found that it is also possible to cause the deposition of glycogen in adipose tissue by the injection of insulin. Whichever method is used, glycogen occurs in brown fat in much greater quantity than in white fat. Animals whose thyroid function has been abolished by thiouracil, and animals which have been castrated, deposit distinctly more glycogen in their brown fat depots than do normal animals under the same experimental conditions. Hence, the amount of glycogen laid down in brown adipose tissue appears to be under the influence of the ductless glands. Similar endocrine effects upon white fat are suspected, but the glycogen content of this type of fat is so small that significant quantitative differences have not been detected by histological methods.

The histochemical reaction of Gomori (3) for lipase was also applied to both types of fat, using as substrates Tween 40, Tween 60, and Product 81. Preliminary observations on the

adipose tissues of well-nourished rats indicate that the subcutaneous white fat of the back is devoid of stainable lipase, while the subjacent interscapular brown fat contains a considerable amount of the enzyme uniformly distributed in the cytoplasm between the lipid vacuoles. The previous observation of Gomori (4), that white fat has a negative histochemical reaction for lipase, is thus confirmed, while the occurrence of this enzyme in brown adipose tissue has been demonstrated histologically for the first time.

Further studies on the variations of lipase content in starvation and hibernation are being undertaken.

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High-Efficiency Counting of Long-lived Radioactive Carbon as CO_2 ¹

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The recent availability of long-lived radioactive carbon (C^{14}) from the Manhattan District (7) in relatively large quantity has tended to emphasize the difficulties inherent in the available methods of measurement of this important isotope. It has been desirable to adapt the Geiger-Müller counter to this measurement. Ionization chambers are not simple instruments to use when connected with sensitive electrometer circuits. Henriques and Margnetti (4) have recently described an ionization chamber used with a Lauritzen electroscope which shows high sensitivity. However, the limiting sensitivity of any method of measurement is determined by the statistics of the backgrounds, which are fundamentally different in counters and ionization chambers. The advantage lies with the counter, as it counts only events, while the ionization chamber integrates the total ionization produced by each event of each kind (2). Counting C^{14} from some solid compound of carbon with thin-window β -counters is at best highly inefficient (8) because of the very low energy of the

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β -ray emitted ($E_{\max} = 0.145$ Mev). Some advantage may be gained by inserting the solid compound within the counter to avoid absorption of the β -rays by the window, as reported by Ruben and Kamen (6), but the efficiency is still limited by the high self-absorption of the β -ray within the solid compound.

In order to avoid the problems associated with the low energy of this disintegration, the obvious solution is to convert the C^{14} to some gaseous compound and use the sample to be measured as the filling gas of the counter. This will allow the handling of large samples with high efficiency. Under these circumstances virtually all of the β -disintegrations will create ionization within the sensitive region of the counter.

TABLE 1
DESCRIPTION OF THE COUNTER TUBES

Counter No.	Length (cm.)	Inside diameter (cm.)	Total volume (ml.)	Cathode length (cm.)	Cathode volume (ml.)	Total volume/cathode volume
18	33	3.8	316	28	301	1.050
19	16	1.2	18.1	13.0	13.5	1.340
20	16	2.1	60.5	14.1	48.8	1.240
22	21	2.1	74.2	18.4	63.7	1.165
23	31	2.1	113.3	28.6	99.2	1.142

The only gaseous compound of carbon into which almost any other carbon compound could be readily converted is CO_2 . However, it has been reported several times that CO_2 is unsuitable as a counter-filling gas because of the complete lack of a plateau in a counter filled with this gas. There are two possible ways to surmount this difficulty: The chemical preparation of the sample may be carried one step further by converting the CO_2 to some other gaseous compound which will have the desirable counting characteristics, or the electrical discharge characteristics of CO_2 may be modified by adding a second component to the counter. As a result of a study of the effect of contaminants on the discharge characteristics of CO_2 (1), carried out in conjunction with the development of a gaseous counting method for C^{14} , a set of circumstances has been found whereby C^{14} may be conveniently and reproducibly measured with high efficiency. Helium, alcohol, ammonia, carbon disulfide, methylene chloride, methyl iodide, ethyl bromide, chloroform, acetone, freon, pyridine, and water have been tried as additives to CO_2 , carbon disulfide being by far the best.

The G-M tubes are conventionally designed glass envelope gamma counter type with a 6-mil. tungsten center wire and a cathode of silver chemically deposited on the inner wall and then coated with colloidal graphite. They are tubulated near one end with a stopcock and ground joint for filling. Counters of a wide range of sizes are found to work well. Those used are described in Table 1. The filling gas is the sample of active CO_2 at any pressure from 10 to 50 cm. Hg with, in all cases, sufficient carbon disulfide vapor to represent 2 cm. pressure within the counter tube. Threshold voltages range from 1,800 to 4,500, depending on counter diameter and CO_2 pressure. The plateau starts at 80–90 volts above threshold, extends for 200 volts, and has a slope of the order of 2 per cent/100 volts. The optimum operating range is about 160 volts above threshold. These counter tubes have been used in conjunction with a stabilized high-voltage power

supply having an output up to 5,000 volts, modified Neher-Pickering preamplifier, scale of 128, Cenco register, and electric timer.

Under these conditions it is found that within these pressure limits the measured counting rate per unit amount of active CO_2 is completely independent of the total pressure of CO_2 and is thus a function only of the amount of activity within the counter tube. It is further found that, if the counting rate is corrected by the ratio of the total volume of the counter to the volume defined by the cylindrical cathode, all counter tubes within the above size range show the same response to equal amounts of activity within the counters. The nonlinearity correction for these counters is relatively large, amount-

TABLE 2
ACTIVITY MEASUREMENTS

Sample No.	$C^{14}O_2$ (micromoles)	CO_2 (millimoles)	Counter No.	CO_2 pressure in counter (cm. Hg)	Threshold voltage	Observed counting rate (c.p.m.)	Background rate (c.p.m.)	Linearity correction factor	Final corrected counting rate	c.p.m. per μ mole $C^{14}O_2$
1	42.2	5.67	18	33.8	4,060	2,090	320	1.000	1,860	44.0
2	36.2	0.159	19	20.1	2,920	1,420	40	1.000	1,850	51.1
3	56.1	3.10	20	9.8	4,320	2,200	70	1.005	2,655	47.3
4	131	1.18	23	21.6	3,555	5,230	159	1.065	6,170	47.1
5	201	1.15	22	34.0	3,720	7,130	99	1.138	9,320	46.3
6	254	3.20	18	20.5	3,540	9,840	301	1.203	12,040	48.8
7	348	0.159	19	52.3	4,390	9,550	39	1.295	16,500	47.4

ing to 12 per cent loss at 10,000 c.p.m. This correction is made from a calibration curve prepared by adding increment amounts of active CO_2 to a counter tube and plotting observed counting rate less background against arbitrary units of active CO_2 in the counter tube.

The measurements presented in Table 2 were made on samples prepared by mixing measured amounts of inert and active CO_2 . The samples of activity were all drawn from the same bulb containing a preparation of radioactive CO_2 . The prepared sample was distilled into a counter tube attached to the glass system with a ground joint by immersing one end of the counter tube in liquid nitrogen. The proper amount of CS_2 vapor to represent 2 cm. pressure in the counter was then added by means of a "doser," after which the counter was detached from the line, allowed to warm to room temperature, placed in a lead housing, the preamplifier leads attached, and the counting rate determined at 160 volts above threshold. Background rate is determined in the same counter filled with inert CO_2 .

The final corrected counting rate is obtained by subtracting background from the observed rate, multiplying this by the ratio of the total volume of the counter to the cathode volume from Table 1 to correct for that fraction of the sample that is not within the sensitive volume of the counter tube, and then correcting this figure for the nonlinearity of the counters with the factor taken from the empirically determined curve previously referred to. The data in the last column of Table 2 show that, with an average deviation of 3 per cent, the system allows the direct comparison of activities of a large range of sample sizes. The sample size range from 0.1 to 9 millimoles of carbon is represented by 10 cm. pressure in the smallest counter to 50 cm. in the largest. In terms of $BaCO_3$, on

which measurements are usually made by solid counting techniques, this represents 20 mg.-2 grams. Sample 7, when removed from the counter, precipitated as BaCO₃ on a 2-cm. filter, and measured on a bell-type β -counter (3) with a 4-mg./cm.² window, gave an observed counting rate, less background, of 50 c.p.m. This is 2.5 \times background as against 250 \times background on the sample when measured as a gas.

While there is no proof in the data that this is an absolute disintegration rate measured by these counters, the fact that the ionizing events registered are those that take place within the cylindrical volume defined by the cathode strongly suggests that the final corrected counting rate is indeed the absolute disintegration rate of the activity within the counter tube. If there were losses, one would expect, from the nature of the discharge avalanche that constitutes the pulse from the counter tube, that these would be greater in the tube of larger diameter. The data on counters Nos. 18 and 19 demonstrate that this is not the case. Thus, measurements on C¹⁴ made in this way, together with the mass spectrometer analysis of C¹⁴ activity preparations, will allow a determination of the presently quite uncertain decay constant of this isotope with an accuracy far greater than is possible by solid counting (5), although this will probably not approach that possible with modern ionization chamber methods after the mean energy of the β -ray is obtained from the spectrum.

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Effect of Flavonols on the Bacteriostatic Action of Dicoumarol

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Goth (3) reported that dicoumarol possessed bacteriostatic action toward certain bacteria which was not antagonized by 2-methyl-1,4-naphthoquinone (vitamin K). This would indicate that dicoumarol exerts its bacteriostatic activity through a mechanism different from that by which it induces hypoprothrombinemia and hemorrhage. In connection with some investigations in progress at this Laboratory (2), it was of interest to determine the effect of compounds containing the γ -pyrone structure on the antibacterial action of dicoumarol. For this purpose we have used the flavonol glycosides, rutin (1) and quercitrin, and the aglycone, quercetin. The effect of rutin

was of especial interest, since it has pronounced physiological activity in diminishing the tendency to hemorrhage by restoring fragile capillaries to normal (4, 5).

The tests were made in nutrient broth (peptone, 0.5 per cent; beef extract, 0.3 per cent; and sodium chloride, 0.5 per cent) adjusted to pH 6.95. Nutrient broth solutions containing desired concentrations of dicoumarol and flavonols were dispensed in 5-ml. quantities in test tubes, sterilized by autoclaving at 15 pounds for 15 minutes, inoculated with 0.01 cc. of a 16-hour broth culture of *Staphylococcus aureus* (F.D.A. 209P), and incubated at 37° C. The antagonistic effect of the flavonols on dicoumarol was determined by using a Klett-Summerson photoelectric colorimeter to measure the density of

TABLE 1
ANTAGONISTIC EFFECT OF RUTIN, QUERCITRIN, AND QUERCETIN ON THE BACTERIOSTATIC ACTIVITY OF DICOUMAROL TOWARD *Staph. aureus*
(Expressed as turbidity readings on Klett-Summerson colorimeter scale)

		Dicoumarol (mg./ml.)			
		0.0	0.02	0.04	0.08
Rutin (mg./ml.; 22 hrs. at 37°C.)	0.0	62	47	0	0
	0.01	66	50	0	0
	0.05	62	58	26	0
	0.5	62	55	59	42
Quercitrin (mg./ml.; 15 hrs. at 37°C.)	0.0	47	27	0	0
	0.05	48	48	35	0
	0.1	52	53	39	21
	0.5	44	38	30	29
	1.0	17	16	13	14
Quercetin (mg./ml.; 19 hrs. at 37°C.)	0.0	45	29	0	0
	0.01	48	42	16	0
	0.05	38	22	13	0
	0.10	0	0	0	0

bacterial growth in the presence of increasing quantities of the flavonols.

The results in Table 1 show that all three flavonols were capable of neutralizing the bacteriostatic action of dicoumarol. The inhibitory effect of 0.04 mg./ml. of dicoumarol was overcome by 0.05 mg./ml. of rutin and completely neutralized by 0.5 mg./ml. Higher concentrations of dicoumarol required increased amounts of rutin to show proportional antagonism. Rutin *per se* does not appear to have any effect on the growth of *Staph. aureus*.

Quercitrin was somewhat less effective than rutin as an antagonist toward dicoumarol. This may be partly due to the fact that in high concentrations quercitrin exhibits toxicity toward *Staph. aureus*. In concentrations up to 0.1 mg./ml. it showed increasing antagonism toward dicoumarol; however, above this value the toxic effect began to show up, and at 1.0 mg./ml. there was a 64 per cent inhibition in the growth of *Staph. aureus*.

Quercetin was the least effective of the three flavonols tested. It did not overcome the bacteriostatic effect of 0.08 mg./ml. of dicoumarol, and showed only partial antagonism to the lower concentrations. It exhibited considerable toxicity toward *Staph. aureus*, completely inhibiting the growth in a concentration of 0.1 mg./ml.

The antibacterial action of quercitrin is probably due to the presence of some quercetin from the hydrolysis of the rhamno-

¹ One of the laboratories of the Bureau of Agricultural and Industrial Chemistry, Agricultural Research Administration, U. S. Department of Agriculture.

side. Investigation of the sample of quercitrin by ultraviolet absorption revealed a small quantity of quercetin. As little as 4-5 per cent of quercetin would be sufficient to produce the degree of bacteriostasis observed in this experiment.

This is the first time that the flavonols have been shown to possess any antibiotic action. The discovery is especially timely, considering the present intensified interest in the subject of antibiotics derived from plants. The results also suggest the possibility of using rutin or the other flavonols to antagonize the hemorrhagic action of dicoumarol *in vivo*.

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The Production of Experimental Pellagra by Adenine¹

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Adenine, linked with other substances, is a constituent of many enzyme systems essential for life and, as a component of the nucleoproteins, is part of the structure of the cell. Many physiological processes are governed by catalysts containing adenine. Presumably, the concentration of free and bound adenine in tissues and body fluids is regulated by a mechanism which determines its formation and utilization, and such a regulation must be of importance to the animal economy.

An attempt was made to disturb this regulation by increasing the concentration of adenine, thereby interfering with the normal metabolism of adenine-containing substances, and of vitamins (especially of the B group), hormones, and enzymes.

Adenine² in the form of the free base alone or mixed with monobasic sodium phosphate ($\text{NaH}_2\text{PO}_4 \cdot \text{H}_2\text{O}$) was given orally, in daily doses ranging from 400 to 500 mg. each, to three dogs over a period of from one to three weeks. The dogs (females) used for the experiments were fed before and during the experiment with K.F.S., Cero Meato (Kennel Food Supply Company, Fairfield, Connecticut), and with Red Heart, Diet B (John Morrell Company, Ottumwa, Iowa). Occasionally this diet was supplemented with milk.

The history of a dog which showed the characteristics common to all three animals given adenine supplemented with phosphate was as follows: Its weight was 11,260 grams;

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² The adenine used in these experiments was supplied by Hoffmann-LaRoche, Inc., through the kindness of Dr. J. A. Aeschlimann.

its age, about three years; time in the laboratory, seven months. The dog was given 400 mg. of adenine and 400 mg. of monobasic sodium phosphate daily in capsules by mouth. Loss of appetite was observed after the second day, and the dog became apathetic. On the fifth day the animal refused all food but continued to take water. The fur looked unkempt, and loss of hair was apparent. The systolic pressure was about 30-35 mm. Hg. above the values found during the control period. On the seventh day along the inner side of the cheeks and the inner upper lips areas of redness were present, stippled with false membrane and disseminated pustules. The tongue was pale grey, and the first quarter of the anterior portion had a brownish-grey appearance. A foul odor from the mouth was evident. The gums bled easily on slight pressure, especially near the alveolar arches of the teeth. Bilaterally, about two inches back from the tip of the tongue on the lateral inferior portion, inflamed areas, about one-half inch long and one-quarter inch wide, were present. The dog vomited occasionally. The systolic pressure was 25 mm. Hg. above the average value for the normal period. At the time of the last dose, given on the ninth day, a marked skin rash was evident, the mouth had a very strong odor, and the entire mouth and pharynx were inflamed. Areas of one-fourth to one-half inch in diameter, covered by a yellowish or yellowish-grey exudate, were present on the inner lips and cheeks, especially at the angle and on the floor of the mouth. Slight pressure on the gums, inner lips, and cheeks produced bleeding. The red line extending along the alveolar arches of the teeth had become a deeper red, and the inflamed areas on the lateral inferior portion of the tongue were covered with an exudate. The tongue had darkened, and the brownish-grey appearance of the anterior-superior portion had extended posteriorly to about two-thirds of its length. The remainder of the tongue was dark grey. The portion close to the tip was almost black and markedly atrophied. Drooling from the mouth was continuous, and the saliva contained some blood. The weakness of the hind legs was pronounced, and the dog staggered when it walked. The cornea of the eye was opaque, giving the iris a spotted, cloudy appearance. The sclera showed marked vascularization. On the margins of the eyelids a yellowish, thick secretion accumulated, causing the lids to adhere.

During the following days the weakness of the animal increased rapidly, and the blood pressure dropped below normal. Voluntary control of the tongue seemed to be almost completely lost. There was an increase in the number and severity of the inflammatory lesions in the mouth and pharynx. Occasionally the dog vomited small amounts of a bloody fluid. The day before the animal died 50 cc. of warm milk was given by stomach tube but was not retained. Death occurred on the 14th day of the experiment, at which time the animal weighed 7,170 grams. The total amount each of adenine and monobasic sodium phosphate given was 3.6 grams. Gross autopsy findings included: alopecia, emaciation, glossitis, gingivitis, stomatitis, congested liver, marked submucosal hemorrhages in the duodenum and marked congestion in the jejunum and ileum, yellowish-grey mottling of the entire surface of the kidney, hemorrhages in the medulla, and bulging of the cut surface.

Two dogs were given a daily dose of 300 mg. of adenine (free base) alone for a period of 21 days. The above-described

signs and symptoms did not develop as fast as when phosphate was added. In addition, these dogs showed spasticity of the jaw muscles and extremities. At autopsy there were, in addition, hemorrhages in the esophagus, more extensive hemorrhages in the small intestines which contained digested blood, hemorrhages in the colon, and slight edema in the walls of the gastrointestinal tract.

Similar experiments were done with young albino rats. Adenine alone (0.5 or 1.0 per cent) or adenine plus phosphate (0.5 or 3.0 per cent) was added to the normal diet. At autopsy the kidneys showed a marked increase in size and weight. The entire surface appeared greyish mottled and hemorrhagic. The cut surface bulged, and the medulla was usually hemorrhagic.

The syndrome produced by adenine points to multiple avitaminosis. It shows all the symptoms described in experimental pellagra in dogs (black tongue). The opalescence of the cornea, the spasticity, and the ataxia observed are characteristic of riboflavin and vitamin A deficiency.

Adenine, or its metabolites, probably produced the syndrome by combining with constituents of the vitamins or their precursors, thus preventing their utilization in the animal. An interference with the formation and activity of alloxazine adenine dinucleotide, of the phosphopyridine dinucleotides (coenzymes I and II), and of nucleoproteins can be assumed. It is of interest to note that a rise in blood pressure resulted and that autopsy revealed extensive damage to the kidney.

These experiments demonstrate the existence of a direct relationship between purine metabolism and avitaminosis. A disturbance of the former may cause changes characteristic of various avitaminoses under dietary conditions which provide for normal vitamin requirements.

If the mechanism demonstrated in these experiments is applicable to human beings, the occurrence of pellagra, which is by far the most frequent variety of avitaminosis occurring in North America, might be reduced and the treatment aided by the elimination of foods containing adenine in a form producing the multiple avitaminosis. To that end the adenine content of certain foods will be determined.

These experiments are being continued and extended to other purines and purine derivatives. A detailed report, including the microscopic findings, will be published elsewhere.

Elasticity of the Aortic Wall

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The rubber-like characteristics of the aortic wall (4, 11) suggest that the wall material is essentially elastomeric. On applying the general theory for ideal elastomers (5), a relation is obtained between relative volume and fluid pressure within a cylindrical tube (7). Some data by Hallock and Benson (3) on segments of the descending human aorta for several age groups were analyzed by means of this relation. In it, the effective thickness, e_0 , was treated as an adjustable parameter and computed for each age group. As anticipated, these values of e_0 were smaller than actual thicknesses, such as measured by Krafka (8) on strips of aortas. It was suggested, however, that

part of this discrepancy is due to a thickening of the aortic wall when peripheral chains are cut. That thickening on cutting does occur was pointed out recently by Remington, Hamilton, and Dow (9). Segments of canine aortas were found to decrease in length by as much as 30 per cent on removal (10), probably in this case due to a shortening of the longitudinal chains. In general, then, intact aortic walls are thinner and less firm than the removed segments.

In their discussion of aortic size, Bazett, Cotton, Laplace, and Scott (1) use values of the ratio of thickness to internal radius of undistended aortas as a function of age which were computed from data obtained by Kani (6). The estimated error in Kani's measurements, however, is greater than the apparent decrease of the ratio with age as reported by Bazett and co-workers for aortas. It is interesting to note that Kani's values for thoracic aortas yield a ratio of thickness to external diameter of 0.088 for the thinnest parts and 0.095 for the thickest parts, with a maximum variation with age of ± 0.008 , only half the estimated average deviation of measurements for any one age group. The corresponding ratio, e_0/d_0 , from the results found in Table 1 (7) are given below:

RATIO e_0/d_0 FOR SEVERAL AGE GROUPS

Age group	20-24	29-31	36-42	47-52	71-78
e_0/d_0	0.094	0.081	0.077	0.073	0.052

The general decrease in the ratio, e_0/d_0 , beyond the age of 20 years suggests that accumulating collagenous fibers and other deposits in the aortic tissues, along with the enlargement of the vessel, cause a thinning out of the elastomeric constituents. Apparently the ratio of actual thickness to diameter remains nearly constant at approximately 0.09, so that by the 75th year almost 50 per cent of the aortic wall is effectively non-elastomeric. On the other hand, the product, $e_0 d_0$, is constant at 15 mm.² to within an average deviation of 0.2 mm.² over the age range of 20-80 years, as though the materials within the vessel wall that render it elastic really do not disappear but, rather, become more thinly dispersed with time (7). Elastin and similar constituents of blood vessel walls are relatively stable substances (2).

From this analysis of aortas the aging process appears, at least in part, to consist of a gradual, effective shortening of molecular chains within the aortic wall. Such an effect can take place either by the establishment of cross-linkages between chains or by introducing fix-points in the form of collagenous fibers and fatty aggregates.

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Undifferentiated Growth of Orchid Embryos on Media Containing Barbiturates¹

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The embryos of orchid seeds are not accompanied by an endosperm or other storage tissue, but are suspended alone in the center of a thin, membranous seed coat. They therefore offer very favorable material for the *in vitro* study of early growth and differentiation. In the course of investigations of the micronutrient requirements of such orchid embryos in pure culture, certain nutrient media containing barbituric acid derivatives were employed. Many of the embryos on these media produced large, undifferentiated cell masses instead of normally organized seedlings. A preliminary account of the appearance and growth of these masses is presented here.

Mature seeds of *Vanda tricolor* were used as embryo sources. The embryos averaged $77\mu \times 197\mu$ in size and contained a total of about 120 cells. There was little evidence of tissue differentiation other than a slightly larger cell size at the basal end. The embryos, with their surrounding testae, were surface-sterilized with a calcium hypochlorite solution and were planted on the surface of solid media in screw-cap containers. Three barbiturates were used: sodium ethyl-(1-methyl-butyl) barbiturate, sodium cyclopentenyl-allyl barbiturate, and phenyl ethyl barbituric acid, each at a concentration of 10 ppm. These were added separately to a basal medium of mineral salts and sucrose, previously reported as favorable for the development of orchid embryos (2). The cultures were maintained in an incubator at 30° C. with a day length of 12 hours provided by Cooper-Hewitt fluorescent lights.

Upon examination after a two-year growth period, it was noted that all of the cultures containing barbiturates showed large numbers of undifferentiated cell masses among the normal plants, while the control cultures with no growth-factor additions showed mostly normal seedlings, with only an occasional embryo with undifferentiated proliferation. The cell masses in the barbiturate cultures were considerably larger than those in the control bottles. The maximum number of cell masses occurred in the cultures with phenyl ethyl barbituric acid. In superficial appearance they resembled the callus tissue of tobacco, described by White (4). The larger masses had a volume of 1.5 cc.; their surface was undulate or pebbled; and they were dark green, pale yellow green, or opaque white in color. There was no external evidence of growing points or other organized meristems. Internal examination revealed a more or less homogeneous cell mass, with no trace of vascular elements or other cell differentiation, except for subsurface patches of meristematic cells. Any given region of meristem apparently functioned only for a brief period, after which it degenerated and was followed by two new meristems, one on each side of the old, thus giving rise to an irregular type of dichotomy. A few of the masses developed absorbing hairs of the sort commonly seen on orchid protocorms. The non-meristematic internal cells presented the same appearance in cross-section as those illustrated by White (4) for hybrid to-

bacco callus, but cell-to-cell differences in size were not as great in the orchid. The nuclei of these cells were very much larger than those in the growing regions and were stained less intensely.

Other instances of abnormal growth of orchid embryos have been reported by Bernard (1) and Knudson (3). In each case the plants showed a marked proliferation of the embryo axis, with several or many growing points instead of the usual single one. They differed sharply from the callus-like masses here reported for barbiturate cultures, in that the multiple growing points soon gave rise to nearly normal stems and leaves and did not continue nonorganized growth.

Attempts to subculture the chlorophyll-containing cell masses of *Vanda* derived from the barbiturate treatment were successful. To date the cultures have gone through five passages of two months each. The rate of growth has remained about constant, with an 8-fold volume increase at each passage, or a total potential increase of 33,000-fold. They thus appear to have an unlimited capacity for proliferation. Preliminary results indicate that the nondifferentiated growth may be maintained on media free from barbiturates.

The abundance of meristematic regions and the occasional presence of a pseudoepidermis with absorbing hairs prohibit the use of the term "tissue-culture" (*sensu strictu*) in connection with these embryo masses, while the lack of organized internal tissue differentiation precludes the use of "organ-culture." In view of their origin, it may be appropriate to designate them as proliferating embryo meristem cultures. The exact relation of the barbiturates to the initiation and maintenance of these cultures is being investigated at present.

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The Inhibitory Effect of Sodium Dodecyl Sulfate Upon the Gastric Secretory Response to Histamine

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We recently reported (4) that sodium dodecyl sulfate in concentrations of 0.1 or 0.5 per cent, introduced into the stomach of the rat, stimulates secretion of the three main components of gastric juice—acid, pepsin, and mucin. In 2 per cent concentration, the alkyl sulfate causes a profuse secretion of mucus only. The selective mucigogue effect of the 2 per cent solution was also observed in the dog (3). To determine whether the 2 per cent solution of sodium dodecyl sulfate failed to stimulate the parietal cells or if it actually inhibited their activity, the effect of this agent on the gastric secretory response to histamine in sacrifice experiments in dogs was studied.

In animals under pentobarbital sodium anesthesia, tracheotomy was performed, the esophagus was tied in the neck, and the pylorus was ligated. A gastric fistula was made, and a catheter sutured into the distal portion of the upper third of

¹ This work was supported by a grant from the Wisconsin Alumni Research Foundation. The barbiturates were supplied through the courtesy of Dr. C. K. Schubert, of Madison.

the duodenum. Three mg. of histamine dihydrochloride were injected subcutaneously at the end of the operation. One hour later and every 15 minutes thereafter for the duration of the experiment, 0.3 mg. of histamine dihydrochloride was injected by the same route. Gastric secretion was collected for half-hour periods for 6 to 9 hours. When the rate of secretion became stabilized, secretions of four 30-minute periods were collected to serve as control samples. The stomach was then filled through the fistula with a 2 per cent aqueous solution of sodium dodecyl sulfate under a pressure of 4 cm. of water. This pressure was maintained for 30 minutes, after which the stomach was emptied, and the collection of samples for 30-minute periods was resumed and continued for four hours. Water and electrolytes lost in the secretion were replaced by the instillation of an isotonic sodium chloride-HCl mixture—through the duodenal catheter. Animals of similar weight and sex, treated identically except that no detergent was instilled into the stomach, served as controls for the maintenance of histamine action. Each sample of secretion was measured and analyzed for free and total acidity by titra-

gastric secretion was represented mostly, and at times exclusively, by mucus. The effect lasted for more than four hours with only slight evidence of recovery of parietal cell activity at the end of that period. Table 1 represents the results of the rates of secretion, concentrations, and output of free acid from two representative experiments.

It is important to note that, in the numerous experiments performed in animals with the pylorus tied, we observed no noticeable change in the gastric mucosa after its exposure to a 2 per cent solution of sodium dodecyl sulfate for two hours in the dog (3) and for six hours in the rat (4). Careful histologic study of the dog's stomach sacrificed at the end of these experiments failed to show the slightest evidence of irritation.

The significance of the inhibitory effect of sodium dodecyl sulfate becomes apparent if it is considered that not only is histamine the most powerful known stimulant of gastric secretion, but also that its action on the acid-producing parietal cell is a selective one. There are reasons to believe that histamine plays an important part in the normal mechanism of gastric secretion as well as in the pathogenesis of peptic ulcer

TABLE 1

Periods.....	1	2	3	4	5	6	7	8	9	10	11	12	13
Control, Dog #9,* M, 7.5 kg.													
Rate of secretion (ml./30 min.)....	6.8	8.0	8.5	8.3	7.0	7.3	8.0	7.0	9.3	9.5	9.5	10.0	10.5
Free acid (meq./l.).....	116	102	116	114	108	115	110	108	111	119	121	119	120
Output HCl (mg./30 min.).....	29	30	36	35	28	31	32	28	38	41	42	43	46
Sodium dodecyl sulfate, Dog #8, M, 7.5 kg.					† 1 hour								
Rate of secretion (ml./30 min.)....	9.3	9.2	9.3	9.9		4.7	3.8	6.0	3.6	3.3	3.3	4.1	4.8
Free acid (meq./l.).....	119	118	123	129		31	28	22	10	3	0	2	9
Output HCl (mg./30 min.).....	40	40	42	47		5.3	3.9	4.8	1.3	0.4	0	0.3	1.6

* Control to show sustained action of histamine upon gastric secretion for duration of experimental period. Actually, a slight rise in secretory rate without drop in concentration of acid toward the end of the experiment is seen, which is rather typical in such experiments.

† Stomach filled with 2 per cent aqueous solution of sodium dodecyl sulfate for 30 minutes. Figures in italics are the results obtained in the periods following the withdrawal of the sodium dodecyl sulfate solution from the stomach.

tion with N/20 NaOH: total chloride, by the method of Wilson and Ball (5); pepsin concentration, by Nierenstein's modification (2) of the Mett method; and mucin, by a colorimetric method developed in our laboratory. The output of hydrochloric acid was calculated for each specimen.

The data obtained show clearly that even relatively short (30-minute) contact with the gastric mucosa of a 2 per cent solution of sodium dodecyl sulfate causes a striking and prolonged reduction of the gastric secretory response to large doses of histamine. Free acidity was actually reduced to zero for a period. The volume of secretion decreased for four hours to approximately 50 per cent (average) of that of the control period. Pepsin concentration remained unchanged, but the concentration of mucin in the secretion was increased considerably (2.5 to 5.2 times). Total chloride concentration decreased from 158-160 meq./l. in the control period to 125-130 meq./l. The latter chloride values are within the range which we previously reported (3) for pure mucus obtained from the dog's stomach. Our results show that parietal cell secretion in the dog, in response to the continued administration of large doses of histamine, is strikingly inhibited by 2 per cent sodium dodecyl sulfate. Under these conditions

in man (1). A few agents are known which can inhibit the action of histamine on gastric secretion, notable among which are preparations of urogastone and enterogastone. However, these agents are effective only when administered parenterally. The marked inhibition of hydrochloric acid production by the alkyl sulfate through contact with the gastric mucosa is of considerable theoretical interest. By increasing mucus secretion and by the inhibition of acid (concentration and rate of secretion) and pepsin (rate of secretion only), therapy with sodium dodecyl sulfate, if conditions for its satisfactory employment for the human subject can be established, would more nearly approach the physiological requirements for the medicinal management of ulcer than any previously recommended form of treatment.

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An Apparatus for the Quantitative Separation of Volatile Substances by Fractionation and Distillation

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An apparatus that has proved useful for the quantitative separation of small quantities of volatile materials in complex pharmaceutical products is here described. As shown in Fig. 1, the apparatus is a combination unit composed of a fractionat-

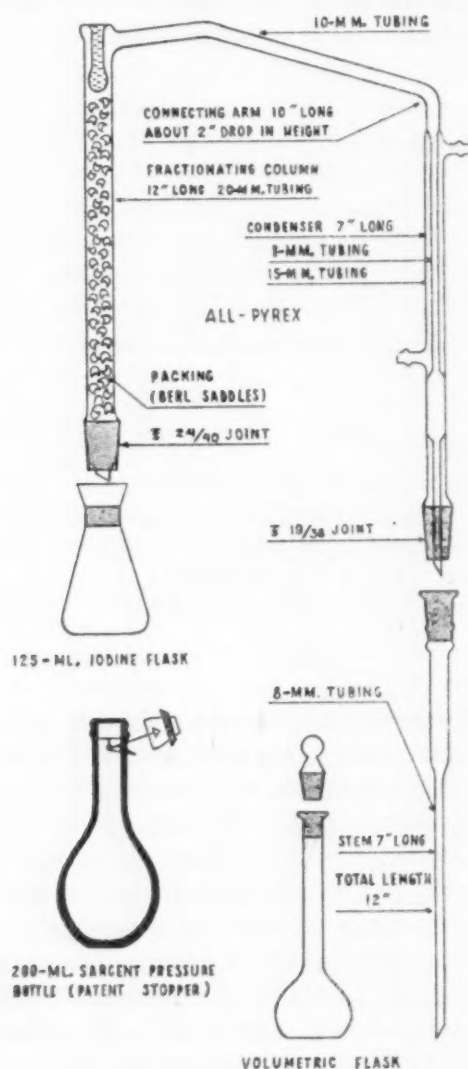


FIG. 1

ing column joined to a condenser by way of sealed glass connections and provided with standard ground-glass joints at the distillation and condenser ends. A small, sealed-in well at the top of the fractionating column, when filled with water, serves to increase the reflux at this point and offers a convenient place in which to insert a small thermometer for measuring the approximate distilling temperature. A 125- or 250-ml. iodine flask (#22 $\frac{1}{2}$ neck) serves as the distillation flask, while a long-stemmed adapter and a long-necked receiving vessel (cooled with ice) are employed at the condenser end. Ceramic

Berl Saddle column packing (6 mm.) is employed in the fractionating column.

Before operation of the apparatus, the flared mouth of the iodine flask is filled with water or some appropriate sealing fluid, and the lower tip of the adapter is submerged about $\frac{1}{4}$ inch in the solvent or reagent placed in the receiving vessel. The ground-glass joints, of course, should be wet before being connected.

The efficiency of the apparatus is largely dependent on the partial vacuum produced during distillation when an appropriate solvent is provided in the receiving flask. This vacuum, caused by the reduction of vapor pressure obtained at the surface of the solvent, is sustained until the adapter is disconnected. As long as ebullition is taking place at a fairly constant rate, an adequate partial vacuum is maintained. Bumping in the distilling flask, prevented mainly by the use of glass beads, etc., causes small variations in the partial vacuum, but the enlarged upper portion of the adapter acts as a safety valve in preventing the distillate from rising too high.

The apparatus has the following advantages: (1) Rapid and quantitative separation of volatile components is obtained. (2) Losses are at a minimum, due to the partial vacuum obtained during distillation, absence of joints in connecting arm, and air-tight connections at distillation and receiving ends. (3) Small amounts of volatile components can be recovered. (4) Standard taper connections permit the use of interchangeable flasks and adapters.

This apparatus has been successfully employed for over two years for the quantitative separation of alcohol, alcohol and ether, and chloroform from pharmaceutical products.

Stability of Penicillin in Glycerin and in Glycols

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Penicillin stability in mixtures containing glycerin (2, 4), propylene glycol (5), or Carbowax (1, 3) (a solid, water-miscible polyethylene glycol) may be less than recent reports would indicate. Since these compounds are major components of such mixtures, penicillin stability in glycerin or glycols alone was determined in order to prognosticate, if possible stability in preparations containing them.

The activity of commercial calcium (CaP), sodium amorphous (NaP), and sodium crystalline (NaP cryst.) salts¹ was determined, before and after storage at 5°, 23°, and 37°C., in glycerin, propylene glycol, and Carbowax,² by the Food and

¹ Pfizer, Heyden, and Commercial Solvents Corporation, respectively.

² Glycerin USP; propylene glycol and Carbowax 1500, Carbide and Carbon Chemicals Corporation.

Drug Administration agar diffusion technic for solutions (6), using the F.D.A. standard penicillin.

As indicated in Table 1, the order of stability at 5°C. is consistently NaP > NaP cryst. > CaP. CaP and NaP cryst.

TABLE 1

STABILITY OF PENICILLIN SALTS IN UNDILUTED VEHICLES

Vehicle	Penicillin salt	Storage temp. (°C.)	Percentage of activity after storage						
			2 hrs.	1 day	2 days	4 days	7 days	13 days	19 days
Glycerin	CaP	5	1	0					
	NaP cryst.	5	2.5	0.7	0				
	NaP	5	14.5		0.1				
Propylene glycol	CaP	5	1.5	0					
	NaP cryst.	5	4	0.05					
	NaP	5	81	67			21	6	
Carbowax	CaP	5	80	27		16	11	2	
	NaP cryst.	5	102	100		96	90	81	69
	" "	23	102	60		44	30	10	4.7
	" "	37	102	55		18	10	0	
	NaP	5	103	104		98	98	98	92
	" "	23	103	100		96	63	38	28
	" "	37	103	86		47	23	2.5	

were almost totally and immediately inactivated in glycerin or propylene glycol, while the rate of inactivation was much less in Carbowax; this was qualitatively true for NaP as well, although inactivation was slower than with the other salts.

In check experiments it was found that absolute (but not relative) inactivation rates varied with the commercial source

TABLE 2

STABILITY OF PENICILLIN SALTS IN FRACTIONS OF PROPYLENE GLYCOL DISTILLATION

Portions	Penicillin salt	Percentage of activity after storage at 5°C.							
		2 hrs.	1 day	2 days	10 days	16 days	29 days	38 days	65 days
I	CaP	80	38	15					
	NaP cryst.	93	91		53	14	8	4	
	NaP	98	100		92	90	81	83	68
II	CaP	50	7	3					
	NaP cryst.	98	101		69	35	23	11	
	NaP	95	100		92	92	91	89	82
III	CaP	0							
	NaP cryst.	2	0						
	NaP	31	20	5					

of glycols, and even with different lots from the same manufacturer. Propylene glycol was accordingly distilled, and penicillin stability determined in three portions: I (the first 25 per cent condensed), II (the next 50 per cent), and III (the residue).

All penicillin salts are more stable in I and II and less stable in the residue than in undistilled propylene glycol. In all fractions the stability order is that derived from Table 1.

Our experience is that penicillin stability varies not only with the vehicle and with the particular salt used, but also with the lot of vehicle, whether or not from the same manu-

facturer. Impurity may be responsible for the latter type of variation. Despite these fluctuations we have found sodium penicillin amorphous most stable and the calcium salt least stable in glycerin and glycols.

Information on penicillin stability is so meager, and in some cases the inactivation so rapid, that assay of the individual preparation is mandatory.

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A Simplified Method of Preparing Active Extracts of B-Glucuronidase¹

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The first procedures published (3, 4) for the preparation of active extracts of β -glucuronidase were tedious and often proved to be unsatisfactory. By employing a new method (1) of obtaining the enzyme from beef spleen, potent highly purified extracts could be prepared with much less difficulty. However, in two steps of the process (acetone precipitation, evaporation of extracts in an air current) there was danger of loss of activity if a certain amount of care was not employed. Another disadvantage was the need for somewhat lengthy large-scale manipulations. For the past several years, one of us (F.) has routinely employed a simplified procedure for preparing small amounts of the enzyme from rat and mouse organs which does not have the disadvantages of the previous method noted above. Extracts of β -glucuronidase prepared in this way have been used in studying the kinetics of the hydrolysis of phenolphthalein glucuronide (5).

Recently, interest has been shown in the use of β -glucuronidase preparations in preference to strong mineral acid for hydrolyzing steroid glucuronides (6) in order to avoid destruction of steroid and prevent the production of artifacts (2). Accordingly, it was felt desirable at this time to report the method of preparation now in use and to present some data on the degree of purification achieved.

Six rats were killed by a blow on the head, and blood was permitted to drain from the carotids. The livers, kidneys, and spleens were rapidly dissected out. These were pooled separately and were homogenized with 100 cc. of cold water in a Waring blender or in a glass homogenizer, and the homogenate strained through cheesecloth (Step 1). The mixture was acidified to pH 5.0 with 1.0 N acetic acid and kept at 38° for 30 minutes. The proteins which flocculated out were removed by rapid centrifugation (20 minutes at 3,500 r.p.m.), and the supernatant separated and preserved. To this fraction was added an equal volume of saturated ammonium sulfate, the mixture then being centrifuged for 30 minutes. The super-

¹ Aided by a grant from the Otho S. A. Sprague Memorial Institute.

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natant was removed by suction and discarded. The residuent was dissolved in 20 or more cc. of water (Step 2), an equal volume of saturated ammonium sulfate solution added, and the resultant precipitate centrifuged off and taken up in a small volume of water (Step 3). Glucuronidase activity was determined on specimens removed at Steps 1, 2, and 3 by the method of Talalay, Fishman, and Huggins (5). Simultaneous determinations of the protein N of the extracts was also performed (1). The results have been arranged in Table 1.

TABLE 1
PARTIAL PURIFICATION OF B-GLUCURONIDASE OF RAT LIVER,
KIDNEY, AND SPLEEN

Total weight of organs (grams)	Fraction	Volume (cc.)	Units*/cc.	Glucuronidase activity (total units)	Units/mg. N
34	Liver 1	117	5,700	673,000	1,160
	2	50	6,240	313,000	3,110
	3	20	15,650	313,000	4,280
6	Kidney 1	96	370	35,500	289
	2	25	488	12,300	665
	3	5	1,630	8,150	2,950
4	Spleen 1	100	1,270	127,000	1,270
	2	25	1,990	49,700	22,300
	3	5	7,280	36,300	18,200

* One unit glucuronidase activity will liberate 1 μ g. of phenolphthalein in 1 hour at 38°C. from phenolphthalein mono- β -glucuronide at pH 4.5 in 0.1 M acetate buffer (5).

Depending on the nature of the tissue being extracted, the activity of the extracts has been increased three to six times, and a 4- to 15-fold purification has been achieved with a preservation of between 23 and 47 per cent of the total original activity. The best purifications were obtained when using spleen, in which the enzyme is present in higher concentration than in either liver or kidney. More powerful preparations were, however, obtained from liver, since this organ contains a greater total amount of enzyme. The application of repeated ammonium sulfate fractionations (1) would lead to much purer preparations of the enzyme. Furthermore, the process could be applied unchanged to larger quantities of tissue so that one could achieve even more potent activities. This has been done using a mixture of livers, spleen, and kidneys from 12 animals. However, where it is not important to have highly purified preparations of the enzyme, the product at Step 3 is quite satisfactory.

The present method eliminates the use of an acetone precipitation and the evaporation of the extract in a current of air, two undesirable operations in the original process. The possibility of undue loss of activity here has accordingly been minimized. This method is also more convenient and more rapid than the previous one, since it requires only a few hours for the complete procedure. Good results have been obtained regularly by those inexperienced in enzyme preparative work.

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Frequency Analysis of Electroencephalograms¹

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Many manual and mechanical types of frequency analyzer are possible, and several have been applied to electroencephalographic problems. The majority are objectionable because they use an arbitrary method of integration, but up to the present time none has received general acceptance and most have been discarded by their authors. It can be presumed that they turned out to be either excessively cumbersome or failed to yield significant information.

Hoagland (9) used a map measurer to determine the length of the contour of slow components in the electroencephalographic tracing. This system required accurate control of amplitude and did not distinguish between amplitude and frequency.

Coordinate graphic analysis has been applied to the EEG (5), but it is such a tedious process that only an inadequate sample is obtainable. For the few seconds of record considered, the method yields an accurate analysis in which phase relations between harmonics are preserved.

Several different types of electrical filters have been used. One system (10) contained constant band-width filters in combination with integrators which measured and recorded amplitude simultaneously. This system was an early prototype of Grey Walter's analyzer and yielded essentially the same type of information. A similar system, employed by Davis (3) and his collaborators, had filters with a band-width proportional to the frequency. These were inserted into the oscillographic recording channels and the amplitude of the various frequency components observed. Six frequency bands could be recorded simultaneously by both systems.

Many recording frequency analyzers have been built in the past for use in sound-wave analysis (e.g. 2, 13).

Before the analyzer designed by one of us (A.M.G., 8) was built, all previous systems of analysis were considered. Experience with the application of filter systems to electroencephalography convinced the authors that complete integration by electromechanical means was necessary and could be accomplished only by a system which made a repetitive function (continuous belt) of the sample chosen. Simultaneous registration of the oscillographic and analyzed records was sacrificed to obtain the highest possible accuracy. It was intended to incorporate this feature at a later date if important information was gained and if further study showed that a loss of accuracy could be tolerated.

In the past six years the EEG's of over 1,000 normal persons and 700 patients with nervous and mental diseases have been analyzed. The instrument used for this work (8) reduces to a spectrum any desired strip of EEG. Such a spectrum is a plot of the alternating-current voltage at any

¹ A grant for the study of this subject was received from the John and Mary R. Markle Foundation. Certain general costs were met out of funds received from the Rockefeller Foundation. The work of reducing data to lists and transforming lists to punch cards was carried out with the aid of the Works Progress Administration under Project No. 17579 and Official Project No. 665-14-3-515.

integral frequency or fraction of an integral frequency between 1 and 60 cycles/second. It was believed that spectrum analysis might reveal significant features of the EEG which had previously escaped attention, and that exact mathematical data regarding the frequency and amplitude of a large number of EEG's would provide a solid objective basis for electroencephalographic diagnosis.

Strips of EEG 30 seconds in length from the frontal, parietal, occipital, and temporal leads (indifferent electrode on the ear lobes) were analyzed. The voltages in each frequency and half-frequency between 1 and 60 cycles/second were read and listed. To facilitate statistical treatment, the data were transferred to IBM punch cards. Three 80-column cards, 10 holes to a column, were used for each spectrum. Since at least 4 spectra were obtained in each case, a minimum of 12 cards/case were required. By running the punch cards through a tabulator, any class of patients or normal controls could be sorted out and the range and distribution of voltage at any integral frequency or half-integral frequency determined. It was an easy matter with an automatic tabulating and calculating machine to obtain averages, mean deviations, and totals of voltage in a wide or narrow frequency range.

Much experimentation with the data finally leads to the conclusion that, although frequency analysis has advantages for revealing certain general features of the EEG, it is not satisfactory for clinical purposes. No index, either simple or complex, based on one or on many spectra from a given case, can express the highly specific detailed information contained in the EEG. Nothing of diagnostic or prognostic significance could be brought out by spectrum analysis that was not readily discernible by an experienced person from inspection of the unanalyzed record.

The reason for the failure of frequency analysis was easier to see by hindsight than by foresight. Such analysis necessarily disregards phase.² In the single unanalyzed tracing, phase is an essential component of wave form. In the multichannel record, it manifests itself as presence or absence of simultaneous, synchronized activity and also as identity or difference in pattern of waves in different leads. These aspects of phase, all taken together, convey a large part of the intelligence in the EEG. Any type of frequency analysis gives a partial expression. It is possible that such an expression might suffice for certain purposes; what was lost might be more than compensated for by an increase in objectivity or ease of quantification. However, experience shows that this is not true for clinical studies.

The analyzer developed by Grey Walter (4, 11, 12) is attractive in that it permits constant registration of alternating-current voltage in various frequency bands, and the registration is superimposed on the unanalyzed EEG. This is merely a practical advantage, however. The analyzer used in our work will integrate the voltage in any selected strip of EEG (7). The length may vary, as desired, from 1 minute to 1 second. The standard integration in most of the work referred to here covered 30 seconds. Moreover, this instrument analyzes the *electroencephalogram*; it is possible to go back over the record and choose for analysis any number of strips, sequence of strips, or overlapping sequence from any lead (7).

² Phase as used here does not refer to the artificial reversal of phase that occurs in bipolar recording when leads are connected from a common electrode (or neighboring electrodes) to opposite inputs of adjacent channels.

Voltage can be read to three places and frequency to 0.1 cycles/second. Thus, this instrument has considerably greater flexibility and resolving power than that used by Walter.

The report by Dawson and Walter (4) gives a satisfactory exposition of the general principles that are subsumed in all forms of sine-wave analysis. However, the authors do not sufficiently stress the fact that to regard the electrical activity of the cortex as composed entirely of sine waves is arbitrary and artificial. The specific nonsinusoidal patterns, illustrated in their report as constructed of sine waves, are so constituted only when the sine-wave components have a specific phase relation to each other. When a method of harmonic analysis disregards phase, it is possible to obtain entirely different nonsinusoidal wave forms with identical sine-wave formulas, as Dawson and Walter show.

Walter and Dovey's report (12) on the value of the frequency analysis for diagnosing deep tumors is unconvincing. The medium low frequency, "gamma," activity which is supposed to indicate a deep tumor is found in many conditions in which there is a slight degree of cortical involvement and is easily seen without an analyzer.

Frequency analysis facilitates the reading of differences in the predominant frequency, but a competent electroencephalographer from casual inspection of the record can read frequency to within 1 cycle/second in the range between 1 and 8 cycles/second and can see all significant differences in frequency above that range, either from measurements of wave lengths or from wave counts. It is possible with proper recording to distinguish at a glance between cortical activity and muscle potentials. This difference is difficult to see on an analyzed record, particularly if the analysis does not extend to 100 cycles/second. A more serious drawback arises, however, from the fact that the EEG cannot be correctly regarded as a repetitive function. The 20-minute multichannel recording with a 2-minute period of hyperventilation, which experience shows is necessary if the EEG is to have approximately full significance, contains thousands of nonrepeating second-to-second variations of extreme importance; because of these transients, each part of the record is different. In essence, therefore, a complete EEG is a large, detailed, and highly complicated picture. The visual analysis and correct interpretation of such a picture is a fairly easy intellectual task; for a machine it is almost impossible.

Improvements will come in electroencephalography when more attention is given to the selection and training of electroencephalographers and to the taking of easily interpreted, undistorted, artifact-free records.³ Considerable skill and much training is required to take a satisfactory EEG. Interpretation requires at least as much intellect and training as general X-ray diagnosis, because the EEG is a registration of a highly complex form of structural functioning more akin to an X-ray picture than to an electrocardiogram. The electroencephalographer must obtain his professional competence by studying for at least a month a large number of normal

³ This means (1) recording that is unaffected by fluctuations in line voltage or changes in temperature, (2) equal amplification of all frequencies between 1 and 80 cycles/second, (3) monopolar recording from at least 8 cortical areas on 6 channels simultaneously (more are desirable), (4) a paper speed of 3 cm./second to give adequate resolution, (5) the center line of each tracing not more than 3 cm. from its neighbor in order to permit close comparison of the activity in neighboring leads, and (6) a record free of artifacts and almost entirely clear of extraneous body potentials.

and abnormal cases in a center where such cases have already been collected and classified. An equivalent training will require 5 or 10 years if the beginner tries to collect the requisite normative and pathological data for himself. He will certainly encumber and embarrass himself if he places major reliance on any type of electromechanical frequency analyzer.

It should not be concluded from these remarks that electromechanical analysis of the EEG is altogether unprofitable. For special purposes and under limited conditions quantification of certain aspects of the EEG is desirable. New types of electromechanical analyzer will doubtless be developed which will be as useful or possibly more so than the one which we have employed or the one devised by Walter. However, experience has shown that in electroencephalography great significance attaches to transient wave forms, wave patterns, and differences in phase relations between leads; for the analysis of this type of data even a supermachine is defective as compared with a trained eye and mind.

Addendum: Since the completion of this manuscript two monographs on frequency analysis of the EEG have been received from France. The first, by Bertrand and Lacape (1), discusses the advantages of graphic Fourier analysis. The second, by Drohocki (6), deals with the electrical activity of the cortex as reviewed through band-pass frequency filters

of the type originally used by Loomis, *et al.* (3, 10). Nothing in these reports requires a modification of the point of view expressed in the present article. Both are valuable contributions but do not consider the limitations of the method employed, nor does either give sufficient credit to the resolving power of the human eye and intellect.

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Book Reviews

Science, liberty and peace. Aldous Huxley. New York-London: Harper, 1946. Pp. 86. \$1.00.

In the second half of the 18th Century and throughout the 19th, many scientists and political philosophers believed that liberty and peace were so linked to science that they must always advance with it. This belief has become constantly harder to hold as the succeeding years have shown a great advance of science with little gain for liberty and less for peace. In the opinion more often expressed today, science is a powerful but morally indifferent engine, which can be used as well to enslave men as to make them free, to kill as to make alive.

This is the opinion of Mr. Huxley in the book here reviewed. But he adds a further and more somber judgment, that the social system under which scientific research began in Europe and, even more, the conditions the world over in which it is practiced today imposed and still impose a tremendous bias toward the use of science for oppression and war.

The book begins with a quotation from Tolstoy: "If the arrangement of society is bad (as ours is) and a small number of people have power over the majority and oppress it, every victory over Nature will inevitably serve only to increase that power and that oppression. This is what is actually happening," to which the author adds: "On many fronts Nature has been conquered; but, as Tolstoy foresaw, man and his liberties have sustained a succession of defeats." To account for this, he says that in the early years of modern

science economic power was already maldistributed. Those who held the greater share of it naturally employed inventors and technologists to apply scientific discoveries in a way to increase their profits and their power. In this way the methods of mass production were improved and those of small production neglected. Consequently, mass production now has an advantage, partly inherent, partly artificial, but able in either case to consolidate more and more power in fewer and fewer hands. Unemployment is both a result and a secondary cause of this concentration. There is now, as there was in the precarious days between the fall of Rome and the rise of feudalism, "a general wish to exchange freedom for protection, independence for guaranteed subsistence in the service of the holders of great power."

Whether this power is held by a ring of financiers or an oligarchy professing socialism is, in the author's view, beside the main point, because the excesses of power will in time mold all oligarchies to a common likeness. And because the craving for power is never satisfied, every such power group will be menaced by every other, and, when it controls the state, it must maintain an armed society. In this its social resources are a hypertrophied industry and fluid labor force, in which both machine parts and people are interchangeable, so that the industry may be quickly converted to the making of munitions and the people readily conscripted and subjected to the mass propaganda of state-worship, an idolatry with practices as revolting as the worship of Moloch.

"The existence of powerful armaments constitutes for their possessors a standing temptation to resort to violence And so long as governments and manufacturers continue to subsidize research into the science and technology of armaments, these temptations will remain. . . ."

Even the fascination of power over the inanimate forces of Nature has, in Mr. Huxley's opinion, contributed to the world's trouble, by leading people to mistake for final reality the restricted aspects of experience, by the study of which scientists have shown how to attain this power. Where scientists, properly for their own purposes, have ignored a part of experience, general opinion has gone farther and denied its existence altogether. This has led to what Mr. Huxley calls "nothing-but" thinking: that "values are nothing but illusions that have somehow got themselves mixed up with our experience of the world; mental happenings are nothing but epiphenomena, produced by and entirely dependent upon physiology; spirituality is nothing but wish fulfillment and misdirected sex." So human values have been debased and the moral forces which might oppose the encroachment of power have been, by this much, weakened.

The author hopes that scientific people will give more care than they have given to the consequences of their work and that inventors and engineers will consciously devote their efforts to those applications of science which favor liberty and peace. Specifically, he hopes for more technical aid to small producers and cooperative enterprises and for research in applied science designed to relieve the economic tensions which menace international peace.

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Butalastic polymers: their preparation and applications.

A treatise on synthetic rubbers. Frederick Marchionna. New York: Reinhold, 1946. Pp. vii + 642. (Illustrated.) \$8.50.

Those familiar with the author's three-volume treatise, *Latex and rubber derivatives and their industrial applications*, are likely to be predisposed favorably to any publication in the field of rubber coming from his pen. The present volume is disappointing despite the worthy objectives which the author has set for himself (pp. 7, 8) and the pleasing arrangement of subject matter in certain chapters, notably Chapters 1, "Historical"; 2, "Butadiene and Its Homologues"; 3, "Halobutadiene Preparation"; 9, "Photochemical Polymerization"; 10, "Polymerization of Haloprene"; 15, "Plastic and Fluid Butalastic Compositions"; and 16, "Filming, Extruding, Coating and Laminating." The skillful rewriting of the patent literature into a volume of ready reference is undoubtedly useful, but this volume is noncritical in that it gives no adequate indication of the relative importance of synthetic rubbers, particularly those which have achieved paramount commercial importance during the present decade.

The book is organized into three major sections apart from an introduction and a brief historical review: Part I, dealing with the source and production of monomers; Part II, with polymerization mechanisms and processes; and Part III, with the properties, processing, compounding, vulcanization, and uses of *butalastics*.

The author chose the term "butalastics" at the suggestion of Ernst A. Hauser, a choice that met the approval of Gustav

Egloff. With this concurrence on the part of specialists in the fields of latex and petroleum, respectively, the die was cast, and future readers of this book will have to struggle with a completely artificial nomenclature woven inextricably throughout the text. The use of terms such as "butalastics-1" for polymers of butadiene or its homologues, "butalastics E" for butyl rubber, "butalastics-3" rather than terpolymers containing one or more butadiene homologues, and "butalastics V" rather than butadiene-vinyl copolymers and homologues, seems confusing and complicated and omits or conceals the familiar names which have achieved wide commercial acceptance.

The reviewer was surprised both to find no mention of GR-S, the Government's styrene copolymer, which for many years has been the mainstay of the whole United Nations' rubber industry, the production of which has exceeded 2,000,000 tons, and to read (p. 8): "The author however, is of the opinion that no matter how good and useful these butalastics are and will be, and how much superior they may be to the natural product in several respects, they will never replace natural rubber in the production of tires which have absorbed for many years more than 68 per cent of the world's production of crude rubber." The facts are that, starting about 1944, 98 per cent of the rubber used in passenger tires was GR-S, and until recently at least 80 per cent of all of the rubber used in the industry has been synthetic.

The literature sources cited include no references subsequent to 1943, and many early patents in the field purportedly covered are omitted.

A United States patent list and three indexes (author, catalysts of polymerizations, and subjects) covering 43 pages have been provided, but the author index does not include all of the authors cited in the text. The subject index is extensive and, with experience, can be used effectively.

Despite the many miscellaneous and interesting items which have been brought together in associations which will provoke reflection and reference to the sources cited, "There are more things in heaven and earth, Horatio, than are dreamt of in your philosophy."

H.L. TRUMBULL

The B. F. Goodrich Company, Akron, Ohio

The production of tobacco. Wightman W. Garner. Philadelphia-Toronto: Blakiston, 1946. Pp. xiii + 516. (Illustrated.) \$4.50.

This book is of world-wide interest and importance not only because tobacco is so extensively used and cultivated but also because of the place it occupies in world trade. The importance of tobacco becomes apparent if it is realized that the aggregate annual production of this crop is about 6,500,000,000 pounds, only about one-quarter of which is grown within the United States.

Since general treatises are available on essentially all other important crops, one may properly inquire why a comprehensive account on tobacco production has previously been lacking. That no one else except Dr. Garner has been qualified to write such a book constitutes the all-sufficient reason. This volume is the product of about 40 years of field and laboratory research and experience. It is truly a monument to the author's broad acquaintance with all phases of the industry, to his incisive scientific judgment, to his painstaking

accuracy in assembling and interpreting data, and to his zealous devotion to fundamental research. It is an invaluable contribution and will satisfy a long-felt need among tobacco specialists, agricultural students, intelligent growers, manufacturers, tobacco dealers, and all others interested in tobacco.

The book is divided into three parts. The first, containing two chapters, deals with botanical aspects of the tobacco plant and its history, and with problems bearing on type, grade, and quality of leaf as related to utilization by manufacturers.

The second part, which constitutes approximately half of the book, is devoted to applied phases of tobacco production. The topics treated in its 12 chapters include varieties, soils, cropping systems, fertilization, seed beds, transplantation, cultivation, harvesting and curing practices, grading and marketing, cost of production of the different types, and important diseases and insect pests.

The third part, containing 9 chapters, deals with the physiology, genetics, and chemistry of the tobacco plant. Herein theoretic considerations and technologic practices are evaluated in such a way as to be of especial value to research workers and manufacturers in all parts of the world.

Dr. Garner has employed ample references and excellent illustrations throughout. Undoubtedly the book will be universally commended as being well balanced, informative, stimulating, very readable, and extremely useful.

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Notes on microscopical technique for zoologists. C. F. A. Pantin. Cambridge, Engl.: at the Univ. Press; New York: Macmillan, 1946. Pp. viii + 75. (Illustrated.) \$1.50.

This little book presents a small number of carefully selected and well-tested methods which the staff of the Department of Zoology, Cambridge University, have found satisfactory for the instruction of advanced students and those commencing research in zoology. We can agree with the author's statement in the Preface: "Experience shows that the student needs some guide through the embarrassing number of methods offered to him by current handbooks of microscopy and histology." The author therefore presents a selection of standard methods, accompanied by lucid but brief comments on their use. In addition, a variety of items of useful information and a small number of important references are presented. The student's knowledge of processes is assumed to be such that definitions can be dispensed with and discussions reduced to a minimum, thus bringing about a great saving of space.

The book is divided into three parts: I, General Methods (53 pp.); II, Special Methods (nervous system, cytoplasmic inclusions, specific constituents, special methods for Protozoa, etc.) (6 pp.); III, Appendix (cultivation of organisms, saline media, physical and chemical data, and preparation of records) (8 pp.). Three pages are devoted to fact and bibliographic indexes.

Beginning graduate students will find in this book a good selection of important methods and references to many special methods which may be needed in certain types of research.

The style is good, and the directions are easy to follow.

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Scientific Book Register

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